Study of Optimal Perimetric Testing In Children (OPTIC)

Dipesh E Patel

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I, Dipesh Patel confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Assessment of the visual field (VF) using perimetry provides valuable information for the diagnosis and management of ophthalmic and neurological disorders. It is estimated that over 3500 children under 16 years of age undergo formal perimetry in the UK per year, without any consensus on approaches to testing in children. There is also a paucity of robust data on the correct interpretation of test reliability, which is necessary to inform understanding of the usefulness of perimetry in monitoring children.

Interpretation of findings relies on an understanding of the normal VF (i.e. reference values), its natural development/progression throughout the life-course and the variability of responses in normal subjects. However there is limited literature in all these areas with respect to children.

To address this, a prospective, clinico-epidemiological, observational study was undertaken, collecting perimetric data on 249 children aged 5-15 years; 154 without an ophthalmic condition affecting the visual field (controls), 65 with glaucoma and 30 with neurological disease. Common adult perimetric tests were used and data on fixation, concentration, behaviour, response to auditory stimuli and fatigue were also collected, to report test reliability.

In a 'normal' population, feasibility and reliability of perimetry improved with age, and by 9 years of age, there were no differences in reliability between tests. 'Good quality' assessments were reproducible on repeat testing. Visual field size/sensitivity increased with age, and reference values were defined for each perimetric test used.

Comparisons between perimeters and test groups highlight differences in test feasibility, reliability and output. Thus, guidance for perimetric testing has been suggested here, including methods for assessing test reliability and appropriate test protocols, dependent on the clinical condition and age of subject.

Follow-up studies are needed to generate the evidence required to understand the role of perimetry in the long-term management of ophthalmic diseases in childhood.

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For Swami,

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Chapter 1 Introduction

The visual field (VF) describes the visual information from an area of space i.e. the spatial extent of an individual's central and peripheral vision. It can be quantified using perimetry, a technique used in a clinical setting to diagnose disease and monitor changes in disease status. The work presented in this thesis comprises an investigation of common perimetric techniques, and their application to the measurement of the visual field in children.

In brief, the next chapter explores the literature surrounding visual field testing in children, identifying gaps within our current understanding. Chapter 3 (pg. 56) then identifies the key study aims to address these gaps. The Study of Optimal Perimetric Testing in Children (OPTIC) (reported in this thesis) is split into three groups, and the reader is presented with methods (pg. 61) and results (pg. 92) for these phases separately. The discussion (pg. 149) synthesises all results, with the ultimate aim of developing guidance for the use of perimetry in clinical practice (pg. 169).

Chapter 2 Background

An overview of current evidence in relation to human visual fields and their assessment is presented in this chapter.

A number of separate electronic literature searches were conducted, targeted to capturing the literature relating to visual field testing in children in general, as well as in childhood glaucoma and neuro-ophthalmic conditions affecting children. The Cochrane Library (Systematic Reviews and Central Databases) was searched, in addition to searches carried out through PubMed (http://www.ncbi.nlm.nih.gov/pubmed), with abstracts searched from 1960 to the present day. These searches were repeated periodically to update with any new evidence, the last search being performed in October 2016.

For the full search terms used, see Appendix I - Systematic review search terms (pg. 184). A full summary of the ophthalmic/perimetric terms used throughout the report are listed in the glossary (pg. 185).

From the literature searches, appropriate titles were identified, and abstracts for these papers were appraised. Full text papers were then retrieved, and further papers identified from their biographies.

Following synthesis of relevant literature, gaps within current knowledge were identified so as to inform the design of the study of Optimal Perimetric Testing In Children (OPTIC), which aims to address key clinical questions relating to the role of perimetry in children.

2.1 The human visual field and its function

The visual field is a term used to describe the visual information gathered from an area of space. It encompasses the entire area that can be seen at any time without moving the eyes.

2.1.1 History of the visual field

One of the earliest recorded accounts of measurement of the visual field and visual field defects was made by Hippocrates (c. 460-370 BCE), recording observations of hemianopia (a loss of sensitivity to light from each eye that corresponds to the same area of visual space). Records of *glaukōma* (glaucoma (known to affect the visual field) – though cataract and glaucoma were not distinguished at that time) have existed since c. 200 BCE, and glaucoma was only recognised as a unique condition by Rufus of Ephesos, c. 100 CE.

For approximately 1000 years, extramission theories of visual perception (where the eye emits light to see) dominated scientific thought. Few philosophers considered peripheral vision though both Ptolemy and Galen penned theories regarding its functioning, thus further recognising the visual field as an aspect of visual function. During the Byzantine Period (after the fall of the Roman Empire) Aëtios of Amida published a chapter (one of eight) solely dedicated to ophthalmology (approx. 550 CE), yet no mention of measurement of visual function was made. For the next millennium, management of eye disease was mainly restricted to herbal ointments and surgical procedures for abscesses and cataract.

In the 1600's there was still no consensus over intra/extramission theories of vision (whether the eye receives or emits light to see). It was common belief that images formed at the optic nerve head gave the best quality vision, yet experimentation led Mariotte (1620-84) to publish 'Nouvelle De´couverte touchant la vue' in 1668 [A New Discovery concerning Vision],[1] describing the association between a 'blind spot' (i.e. an area within the visual field that does not perceive light) and a physical structure within the eye – the optic nerve head. Further development of ophthalmic tools allowed Albrecht von Graefe (c. 1850) to observe papilloedema (swelling of the optic disc) in subjects with raised intracranial pressure secondary to brain tumours and thus recommend the observation of the optic nerve head as a diagnostic tool.

Though it is possible to track observations of visual field measurement and detection of defects throughout history, it is evident that landmark changes in understanding visual function took over 2000 years to come to fruition. Throughout this period, advances in areas of medical and imaging techniques have allowed progression in our understanding of the visual field and strengthened links between anatomy and function.

In the early 20th century, large advances were made in understanding the importance of monitoring visual fields in the management of ophthalmic disease,[2-8] leading to the development of perimetry in the form as we know it today.

However, recent evidence shows that structure/function relationships are not perfectly correlated[9-13] and thus the role of monitoring visual fields is an

independent, established mode of monitoring ophthalmic/neuro-ophthalmic disease in adults.

The following sections will examine perimetry in depth, followed by current literature relating to perimetry in children and specific childhood ophthalmic diseases that affect the visual field.

2.2 Assessment of visual field function (perimetry)

Formal assessment of the visual field looks at a combination of factors, comprising:

- **Sensitivity** – measured in decibels (dB – a logarithmic unit used to express a ratio) – The ability to detect a 'light' target of a set size/intensity at a location within the visual field
- **Size** – measured in deg/deg^2 – The extent of the visual field or its area
- **Shape** – The overall shape of the visual field, particularly any changes in shape characteristic of disease

Testing of the visual field can produce an asymmetric 'hill of vision' sensitivity map for each eye (Figure 1, pg. 21). This demonstrates how sensitivity to light reduces as eccentricity (distance from the fovea, commonly measured in degrees) increases, with sensitivity in the temporal field still present at extreme eccentricity.

Although each individual field varies slightly in shape and size, adult visual fields commonly extend to 60° superiorly, 75° inferiorly, 100° to the temporal side and 60° to the nasal side[14, 15] from the centre of the field. Within this field, each location

has a certain degree of sensitivity to light, which reduces when moving further away from the fovea (at the centre of the field).

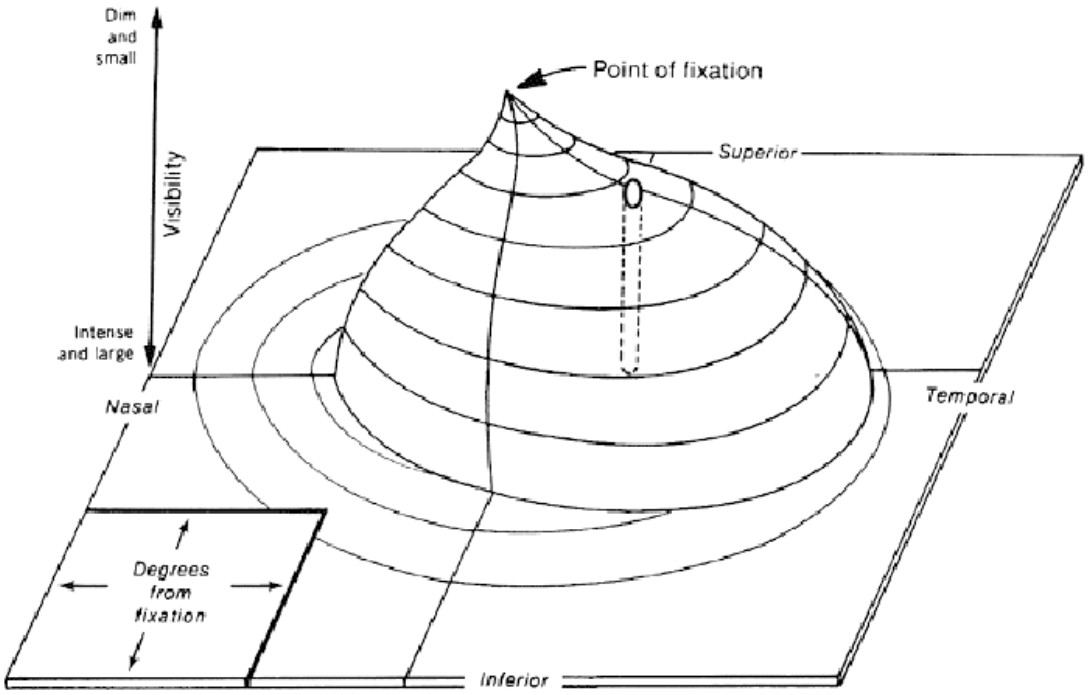


Fig. 2. The normal island of vision. The hill is highest at fixation, where visual sensitivity is greatest. The height of the hill of vision declines toward the periphery as visual sensitivity diminishes. (Anderson DR: Perimetry with and without automation, 2nd ed. St. Louis, CV Mosby, 1987)

Figure 1. 'Hill of vision' sensitivity map

2.3 Perimetry in children

2.3.1 Visual field testing equipment

Visual field testing – perimetry – in adults is commonly performed using specialised equipment (perimeters, Figure 4-Figure 6, pg. 30). The testing 'face' (surface) is bowl-shaped (testing using a flat surface is referred to as campimetry), but otherwise perimeters vary in design and testing algorithms available. They use an adjustable 'chinrest' and forehead bar to keep subjects aligned and still throughout testing. Responses are recorded by the subject pressing a handheld

buzzer when a target is perceived. The targets either flash (static perimetry) or move (kinetic perimetry).

A summary of the most common perimeters used in the UK hospital eye service are shown below (Table 1, pg. 23) along with other methods of assessment that are not based on the use of a standard bowl perimeter (Table 2, pg. 24). Images of the three most common bowl perimeters are also shown below (Figure 4-6, pg. 30) and a detailed overview of how different visual field testing modalities (static and kinetic) assess visual field (VF) sensitivity, size and shape is reported below.

Table 1. Conventional perimetric techniques

Conventional perimeters	Function assessed	Extent of VF tested	Algorithms	Post-hoc sensitivity adjustments	Experienced perimetrist required?
Humphrey Visual Field Analyzer (static perimeter)	Sensitivity at pre-defined locations	Central 24°/30° Full-field	Full threshold SITA* SITA FAST C-40 (supra-threshold) Estermann	Yes	No
Goldmann perimeter	VF Size VF Shape Sensitivity to a set intensity of light (multiple locations)	Full field up to 90° for horizontal meridia, and approx. 70° for vertical meridia	N/A	No	Yes
Octopus static perimetry	Sensitivity at pre-defined locations	Central 30° Full-field	G – TOP^ G GATE#	Yes	No
Octopus kinetic perimetry	VF Size VF Shape Sensitivity to a set intensity of light (multiple locations)	Full field up to 90° for horizontal meridia, and approx. 70° for vertical meridia	N/A (Test patterns can be pre-set and saved)	No (reaction time correction available)	Yes

*Swedish Interactive Thresholding Algorithms (SITA). ^Tendency Oriented Perimetry (TOP). #German Adaptive Thresholding Estimation (GATE)

Table 2. Qualitative and emerging perimetric techniques

Novel / qualitative techniques	Function assessed	Extent of VF tested	Algorithms	Post-hoc sensitivity adjustments	Experienced perimetrist required?
Fields to Confrontation	Gross sensitivity (qualitative)	Full field	N/A	N/A	Yes
Saccadic Vector Optokinetic Perimetry (SVOP)	Supra-threshold sensitivity at pre-defined locations	Central 25°	Supra-threshold (binocular/monocular)	No	No

2.3.2 Mechanisms of formal perimetry

Bowl perimeters can usually be used to perform multiple types of assessment, as described below, together with an exploration of the utility of these in relation to assessing visual fields in children.

2.3.2.1 Static perimetry

Static perimetry is fully automated and, with a co-operative subject, can be conducted by an inexperienced examiner.

a) **Static threshold perimetry** assesses the ***sensitivity*** to **flashes of light** of ***varying intensity*** **at a fixed location**. It is therefore only possible to test a small area of the visual field before fatigue effects make further testing unreliable.[16] Adults with glaucoma have been shown to demonstrate a much higher loss of sensitivity with increasing test duration compared to controls.[17] To mitigate these effects, automated static perimeters use algorithms designed to shorten test duration and improve reproducibility, compared to the older method of 'full-threshold' testing. The most commonly used, the Swedish Interactive Thresholding Algorithms (SITA) for the Humphrey Field Analyzer (HFA, Carl Zeiss Meditec VG mbH, Germany), presents 25-30% fewer test stimuli[18] and reduces test duration by 50% in normal adult subjects[19] and 54% in adults with glaucoma,[20] when compared to full threshold testing. As well as generating sensitivity values, these algorithms also report summaries of the visual field, comparing the tested field to an underlying normative database. These include 'mean deviation' (MD), a measure of how far the measured

sensitivity in an assessment deviates from an expected value. Other values include pattern standard deviation (PSD), the Glaucoma Hemifield Test (GHT), and visual field index (VFI). These terms are explained in more detail in the Glossary (pg. 185). Automated static perimeters can also produce reliability measures based on fixation losses, false positive and false negative responses.

b) Static perimetry can also be performed as a **'supra-threshold'** screening examination. This uses stimuli of a ***set size and intensity*** at **fixed locations** and registers responses as either 'seen' or 'not seen'. Unlike threshold perimetry this does not measure the actual limit of a subject's sensitivity.

2.3.2.2 Kinetic perimetry

Kinetic perimetry assesses the ***location*** at which a **moving light** stimulus of a **fixed size/intensity** can be seen. This allows for testing over a larger area of the visual field. Targets are presented centripetally, along a number of meridians (Figure 2, pg. 27). Responses are then plotted and joined forming an 'isopter' (maroon line, Figure 2). The isopter depicts the first point at which a particular target is perceived i.e. a line of differential light sensitivity (DLS). Within the area delineated by the isopter, the subject is able to see the target. Outside of the line, it is beyond their sensitivity and they cannot perceive it.

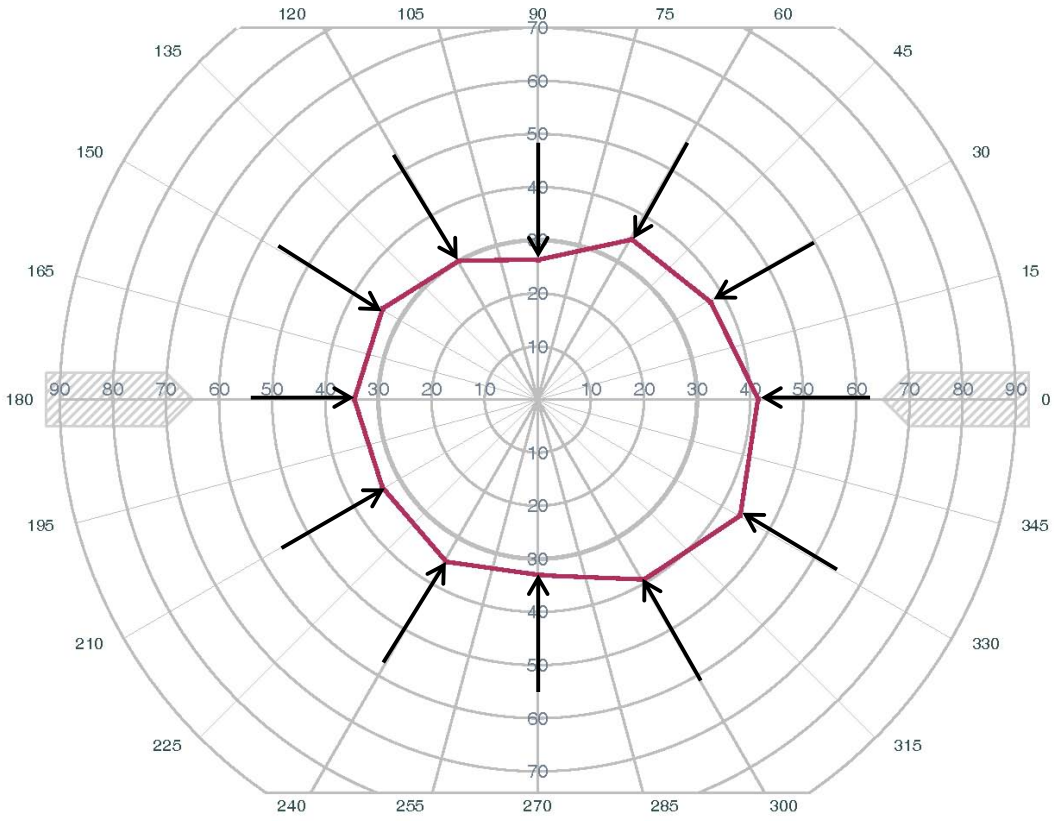


Figure 2. Formation of a kinetic isopter

The standard measure for stimulus sizes used in kinetic perimetry was developed by Goldmann, and uses six sizes; 0 to V, ranging from 0.0625mm^2 for size 0, to 64mm^2 for size V. The most common test size (I) is 0.25mm^2. Stimulus intensity is divided by 'major' and 'minor' filters, using numbers 1 to 4 and letters 'a' to 'e' respectively. Thus, the largest, brightest stimulus is V4e, whilst the smallest, dimmest stimulus is 01a.

Figure 3 (below) shows kinetic perimetry with multiple isopters, using different stimulus sizes/intensities. This approach allows for extensive assessment of the visual field, but requires a longer test duration.

The inner isopter (maroon, I2e) uses a small, dim light. The outer isopter (black, III4e) uses a large, bright light and can therefore be detected much further into the

peripheral field. Kinetic perimetry also assesses the size, shape and location of the blind spot. The blind spot is an area of the visual field that is not sensitive to light (Figure 3, pg. 29). Anatomically, this is the location of the optic nerve head on the retina where nerve fibres leave the eye and travel to the visual cortex via the visual pathway. Kinetic perimetry requires an experienced examiner to perform and document the assessment. It also allows for flexibility and responsiveness by the examiner and is therefore considered particularly useful in the assessment of children.

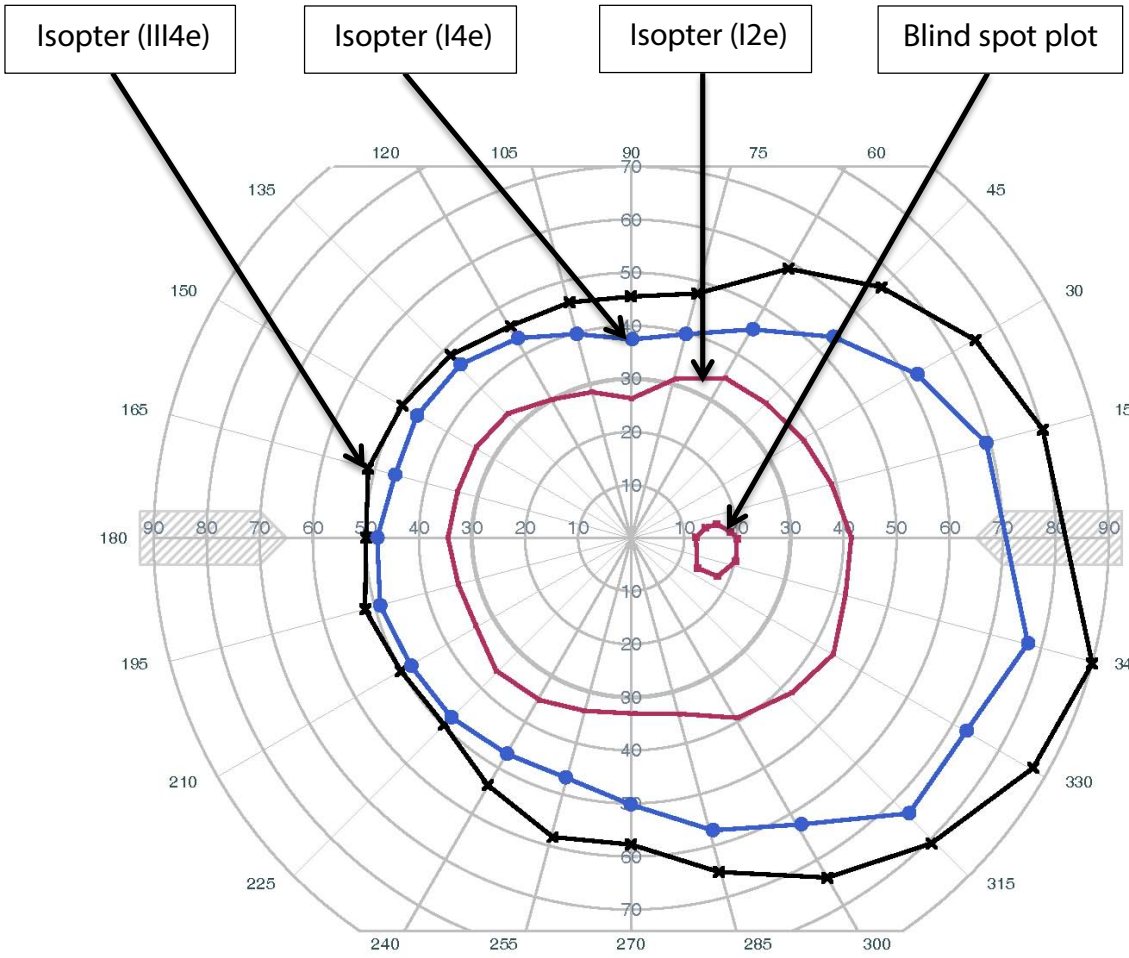


Figure 3. Kinetic perimetry using multiple isopters and a blind spot plot

2.3.2.3 Summary

Both static and kinetic techniques allow for mapping of sensitivity in the visual field, but given the techniques used to capture information are fundamentally different, they can be considered to be measuring different aspects of visual field function. This commonly translates into their use in detecting visual field defects of differing aetiology in clinical practice, as discussed later.

www.meditec.zeiss.com

Figure 4. The Humphrey Visual Field Analyzer

(Vaughan et al, 1999[21])

Figure 5. The Goldmann perimeter

www.haag-streit-usa.com

Figure 6. The Octopus 900 perimeter

2.3.3 Visual field testing strategies in children

In this section, current evidence within the field of perimetry in children is summarised and the rationale for the research presented in this thesis is discussed.

When assessing visual fields in children, there are four groups of tests available to use (conventional perimetry, qualitative assessments, novel techniques and objective assessments). The merits and weaknesses of these are discussed below.

2.3.3.1 Conventional perimetry

Firstly, as reported earlier, there are a number of perimeters and testing strategies that assess static perimetry to threshold, as well as conventional kinetic perimetry performed on a Goldmann perimeter. These tests have the benefit of an extensive underlying evidence base,[18-20, 22-35] albeit mostly in relation to perimetry in adults only. These perimeters are present in hospital eye services around the world, and are therefore accessible to clinicians. However, there is limited guidance on their use in children, particularly for children under 8 years of age.

Interpretation of findings relies on an understanding of the normal visual field (VF) (i.e. reference values), natural development/progression throughout the life-course[36] and the variability of responses in normal subjects.[26] Each perimeter has a normative database against which a patient is compared, yet these databases were not developed for/by testing of children. The effects of testing children and mapping their data to an adult reference are poorly understood, and findings differ according to the test algorithm and examination technique used.[37, 38] Thus,

there is little guidance available on interpretation of VF data in children, particularly for common static test strategies.

2.3.3.1.1 Kinetic perimetry

The Goldmann perimeter was first produced in the 1940's[39] and is still widely used in current paediatric practice[40] because of its accuracy, flexibility and full-field testing capability. For these reasons, it is still regarded as the clinical 'gold-standard' perimeter for use in neuro-ophthalmic practice. However it is no longer commercially available and with time, as equipment fails and is replaced by other perimeters, it will no longer be widely available for clinical use. Octopus perimeters have been available in a clinical setting for many decades, and their use is well established in Europe and the US. The perimeters are updated regularly, and the latest version of the perimeter, the Octopus 900, is now commonly used in the EU and UK. The new Octopus offers full-field kinetic perimetry akin to Goldmann perimetry.

More recently, third-party replacement models have been developed to replace the Goldmann. These have almost identical specifications, but as yet, there is no literature available to support their use in practice. Two available options (the Inami L-1550 and Takagi MT-325 UD) are shown below (Figure 7Figure 8).

http://inami.co.jp/en/

Figure 7. The Inami L-1550

http://www.takagieurope.com/

Figure 8. The Takagi MT-325UD

Historically, Goldmann kinetic field testing started with plotting of the blind spot, followed by mapping of the central visual field area. This was performed with a stimulus that was only just perceivable at 30° eccentricity and allowed the examiner to continue an assessment with any necessary refractive error correction in place. The outer visual field was then plotted, using a larger/brighter stimulus.[14, 41] Other methods of assessment start by plotting the far-peripheral field first, thus familiarising subjects using a stimulus that is easier to detect. The speed of target

presentation is recommended at 2 to 3°/sec.[41, 42] Unlike automated perimeters, kinetic perimetry outputs do not have automatically generated reliability indices, making rapid evaluation of visual field test reliability impossible without examiner comments.

Prior studies have often tested feasibility of Goldmann perimetry using single isopters with large stimuli (i.e. V4e or III4e) along limited test meridians, limiting their ability to inform clinical practice.[43-46] Semi-automated kinetic perimetry (Octopus 900) is reported to be feasible in children.[35] However there is no evidence regarding its comparative feasibility and reliability, which is necessary to understand whether the Octopus can reliably replace the Goldmann as the perimeter of choice in children.

2.3.3.1.2 Static perimetry

The first static automated perimeters used algorithms that involved very long test durations. In 1995, before shorter algorithms (SITA) were created, one study found that 40% of children aged 6 to 11 years with congenital glaucoma could not complete a Humphrey 24-2 assessment.[47] Since the advent of newer, shorter algorithms, a recent study of practice found that the Humphrey SITA algorithms are now the most commonly used assessments in children in the UK.[40]

There is evidence to suggest that assessment of children (aged 6-13 years) with the HFA (SITA FAST strategy) yields reliable responses (as assessed with automated reliability measures of false positives, false negatives and fixation losses) whilst being one of the shortest test algorithms.[45] SITA testing has been

compared to full threshold testing in children, with the SITA algorithm yielding results in 50% shorter duration, with less intra-test variability.[48]

Previous studies have used a variety of methods for measuring reliability of perimetry in children, ranging from automated reliability indices to custom qualitative examiner report, making comparisons between studies difficult. Reliable subjective responses have been found in children aged 7 to 8 years[49, 50] (using rarebit/frequency-doubling perimetry and tendency oriented perimetry (TOP) respectively). Reliability using continuous light increment perimetry (CLIP) improves with age, and reaches adult-levels at 13 years,[51] yet these techniques are not widely adopted in clinical practice.

The reliability of static perimetry in adults is assessed using reliability indices (RI's). These consist of false positive responses, false negative responses and fixation losses. These measures are reported with the output of every visual field test and provide a fast method for assessing visual field reliability. The appropriateness of applying these measures to children has not been reported in the literature, yet it is critically important when testing children to be able to detect when a visual field test is unreliable.

Overall, there is still a paucity of robust studies comparing perimetric testing strategies in children, both with and without ophthalmic disease. This lack of evidence means clinicians do not have sufficient knowledge to inform selection of an appropriate visual field test, nor have available age-matched normative data i.e. expected values, with which to compare test results of their patients.

2.3.3.2 Qualitative assessments

The second widespread approach to visual field assessment is the method of 'confrontation' field testing. This method does not require specialist equipment and can identify gross visual field defects, but requires an experienced examiner. Clinically, this method is used where formal perimetry is impossible e.g. in children too young to co-operate or in adults with severe cognitive impairment.

2.3.3.3 Novel techniques

The third group comprises a variety of novel perimetric tests designed to aid assessment in the very young, those with short attention spans and those unable to fully comprehend complex instructions. Three approaches of particular note assess visual fields using supra-threshold stimuli (i.e. those that do not test actual sensitivity). The oldest test uses an adapted Goldmann perimeter, fitted with pulsing light emitting diodes (LEDs) to perform a test of sensitivity every 7° along 24 meridian.[52] This test has been successfully performed in infants as young as 6 months of age.

The latest supra-threshold visual field tests for children have been designed using newer technology and also benefit from allowing children to sit and perform the test without using a chinrest. They can incorporate a computer game element or cartoons to aid with compliance. When compared to confrontational field testing, the 'KidzEyez' test showed a 100% sensitivity and specificity.[53] This test is based on the use of a large plasma screen, presenting cartoons centrally, with small, intermittent peripheral targets presented to assess peripheral sensitivity. Reponses are monitored via manual (video) eye tracking. Saccadic Vector

Optokinetic Perimetry (SVOP) follows a similar testing protocol, but with automated eye-tracking, and has shown a 99.1% agreement with the Humphrey C-40 screening test in children aged 5-9 years without eye conditions.[54] However, recent evidence has shown agreement between SVOP and Goldmann perimetry as 64.7%, with poor testability, and limited ability to calibrate eye tracking in children with corneal changes seen in childhood glaucoma.[55] Both of these assessments have yet to be fully validated, but could hold promise for supra-threshold testing in a limited group of young children in the future. Whilst supra-threshold testing is beneficial for initial detection of moderate visual field defects, it is more difficult to use in monitoring for small changes/progression as it cannot detect any change in sensitivity until the sensitivity drops beyond the threshold being tested.

2.3.3.4 Objective assessments

The final group of tests do not rely on subjective responses. Measurement of visual evoked potentials (VEPs) can be used to assess visual field function in this manner, however it is generally limited to testing near the centre of the visual field[56, 57] and has been shown to falsely classify normal fields as pathological in 42% of adult cases.[58] To assess VEPs, electrodes are placed on the subjects head and these record electrical responses over the visual cortex when a subject is shown a visual stimulus. VEPs have been shown to be unaffected by divided attention and other on-going mental processes,[56] which may make them a suitable choice for testing children with poor attention, but requiring careful interpretation of findings.

Another objective measure of visual field function comes from assessments using pupillometry[59] i.e. a change in pupil diameter when presented with a peripheral stimulus. This technique has been shown to be reasonably successful at detecting glaucomatous damage in adults, with agreement with perimetry in 70% of eyes.[60]

2.3.4 Potential sources of variation/error specific to perimetry in children

As discussed earlier, the assessment of a child is different to that of an adult. As well as the need to consider and allow for sources of error known in adult perimetry, the examiner must be mindful of additional challenges in testing a child.

As well as selecting an appropriate visual field test, it is also important to give clear, concise instructions to child subjects, to avoid misinterpretation of the task. One study[61] examined perimetry preparation tasks in children aged 5-8 years, reporting that these young children are able to perform automated perimetry and performance improves with training, with older children requiring less training. They also noted that there was large intra-group variability in 5 year old children; some managed the task well, and others struggled, suggesting that results in young children depend largely on the general behaviour and capability of the individual child. One study highlights the positive influence of parents in the room during testing to help reassure young children (it is mandatory in the UK to have a chaperone present) and the use of frequent verbal encouragement during the test.[50] Children have also been noted to have naturally high false positive responses, and should be encouraged to only respond when a test stimulus is perceived.[62]

Whilst giving comprehensive instructions, it is also important to ensure children are not overburdened with information.[61] Adults are commonly warned about blinking during perimetric testing, yet blinking during perimetric assessments does not affect threshold variability of static perimetry, and evidence suggests that people naturally blink after they respond to a supra-threshold stimulus.[63]

Children with neurological visual field defects can develop compensatory mechanisms to search the 'blind' visual field.[64] These mechanisms can interfere with perimetry when the subject constantly attempts to search the damaged area of the visual field during perimetric testing,[65] thereby plotting the 'functional' visual field rather than the true 'anatomical' visual field. As in all children, constant reminders to maintain central fixation are very important.

When measured with a custom, research-based perimeter, children with Autistic Spectrum Disorder (ASD) have been shown to have reduced visual field sensitivity, particularly in the nasal field.[66] Interpretation of findings in these children should account for this, though the extent of loss as measured by conventional perimetry is unknown.

In a small series (*n*=55), adults undergoing perimetry were assessed for symptoms of ocular rivalry arising from occlusion of an eye. 44% reported symptoms, but symptoms were shown to have no effect on visual field test results.[67] Symptoms of rivalry may distract children, but they can be re-assured that this phenomenon is normal and won't affect their test results.

Finally, correction of refractive errors in perimetry is essential to ensure accurate information is collected about visual field sensitivity. Uncorrected myopia has a

greater impact than uncorrected hypermetropia,[68] although generally it is advised that any refractive error should be corrected for testing visual fields within the central 30°, with additional hyperopic correction for presbyopia.[41] Whilst uncorrected refractive error causes defocus, and therefore reduced sensitivity, it does not increase the variability of responses.[69] For kinetic perimetry, peripheral stimuli usually remain uncorrected. One study has shown that the I4e stimulus is affected by refractive errors more extreme than -18D or +13D. The III4e and V4e stimuli remain unaffected by any refractive error between -25D and +17.25D.[70]

2.3.4.1 Summary

Given this evidence, there are behaviours that should be monitored carefully when assessing visual fields in children (e.g. responses to stimuli), in order to achieve a result representative of a child's visual function.

2.4 Development of the visual field

A summary of literature on the development of the visual field, and on normative fields in children will be covered in this section. The limited literature suggests that visual fields develop rapidly with age in the first few months of life, with the temporal field developing faster than the nasal field.[71] There is still considerable debate as to when visual fields become fully 'mature' in terms of sensitivity, area and shape, with some reports suggesting this may occur as early as 6 months of age,[52] and others providing evidence of maturity occurring anywhere between 2 and 15 years.[43, 44, 72, 73] Reported studies have employed a wide range of perimeters, testing strategies and novel/research techniques, which accounts for some of the differences in results.

One study reported trends for increasing isopter size with age and repeat testing, but these did not reach statistical significance.[74] It is possible that due to small sample sizes in the studies above, they have limited power to detect associations between variables such as visual field size and age.

Further variability is introduced by subjectively assessing young children. Given the lack of consensus on the age of visual field maturation it is important to have established normative values for commonly used perimeters, specific to the algorithm used, and including a wide age range.

2.5 Current literature on normative visual fields in children

Throughout the literature perimetric data have been presented in different ways, which makes it difficult to draw comparisons between studies. Furthermore, visual field textbooks commonly present a sample normal field of an adult for reference and do not describe normative fields in children.[14, 41, 42] Normative fields have been documented in adults using Goldmann perimetry. There is sparse literature on normative values for children of visual field sensitivity and extent using commonly used perimeters. The Octopus perimeter uses a normative database from an adult sample to draw reaction-time corrected isopters for the kinetic programme.[38] The underlying database groups subjects in 10-year age bands (10-20 years up to 70-80 years) with only 12 participants (mean age 14.1 years) in the youngest age band. Thus, currently, findings in young children assessed with Octopus kinetic perimetry are compared to a normative database of much older children i.e. without taking account of developmental changes.

There are data available from a single study of the development of normal visual fields in children measured using kinetic perimetry, with double arc and Goldmann perimeters.[43] That study only measured visual field extent along 4 meridians, and therefore provides limited information on change in visual field shape with age. Another paper demonstrates a change in visual field size with age using a large sample of 374 subjects, comprising a baseline of 14-15 year olds, and adult subjects between 20-69 years of age.[36] This paper also describes a level of 'tolerance' for normal visual fields, which is approximately 10-15° wide per isopter, but uses a method of analysis that pre-dates modern techniques. The most recent paper describing normative adult visual fields (*n*=22) uses a more conventional ±2 SD around a mean value.[37] However, this gives a large range of normality that spans >30° for some points. It is therefore extremely difficult to predict the appearance of a normative response from a child or base a power calculation on adult values.

Humphrey SITA 24-2 FAST testing in normal children has shown a mean deviation (MD) from the normative database used as –4.1 +/- 1.3, –3.1 +/- 0.9, –2.3 +/-0.6 and –1.9 +/- 0.4 dB, in 6-, 7-, 8- and 9-year-old children respectively (p=0.001).[45] These data are suggestive of an increase in visual field sensitivity with age.

2.5.1.1 Summary

There is currently limited evidence that describes normative visual fields in children, across a range of perimeters. Current literature often pertains to adults only, and it is not known if it is appropriate to infer from standards used in adults.

Thus, age-appropriate normative values are very important to determine in children, as they are the basis of ruling-in/ruling-out visual field defects at different ages.

2.6 Visual fields in subjects with refractive error, amblyopia and strabismus

Children with neuro-ophthalmic disease and childhood onset glaucoma, in whom assessment of the visual field is important, are known to have a higher prevalence of refractive error, strabismus and amblyopia compared to the wider population. It is therefore essential to understand any effect of these conditions themselves on the visual field, including whether the visual fields are the same in the amblyopic and 'fellow' eye.

Whilst uncorrected refractive error can impact on the findings of perimetry, correcting refractive error can also induce difficulties. There are studies reporting the risk of lens artefacts with incorrectly placed lens holders[75, 76] and prismatic effects when correcting refractive error in aphakia.[77] Careful alignment of a subject can mitigate these effects, although contact lens wear is preferable if available.

Amblyopia is known to cause a range of perceptual abnormalities including abnormal spatial resolution, contrast sensitivity[78] and visual evoked potentials. It can also cause positional uncertainty and eye movement abnormalities. These effects have been reported for the amblyopic eye, but 'fellow' eyes in children can also have reduced contrast sensitivity function,[79, 80] acuity[81] and horizontal eccentricity of fixation.[82] Amblyopic and fellow eyes have also been shown to demonstrate altered foveal structure compared to normals.[83]

The central visual field of amblyopic eyes has been shown to have a reduced sensitivity,[84, 85] but this does not extend to the far peripheral field. Macaque monkeys with naturally occurring strabismus have been shown to have reduced visual fields in their temporal field,[86] and eyelid suturing at various stages of visual development causes variable degrees of visual field loss,[87] whilst squirrel monkeys deprived of any visual stimulation in one eye show complete loss of visual field function.[88]

There is evidence of differences within the peripheral field between amblyopic and fellow eyes, consisting of lower peak contrast sensitivity in the central 30° of the amblyopic eye field. This phenomenon persists for all sine grating stimulus field sizes in the peripheral field, but sensitivity to large field sizes improves in amblyopic eyes when presented in the centre of the field.[89]

Assessment of fixing eyes in children with strabismus suggest there are no differences in visual field sensitivity compared to 'normal' eyes using kinetic perimetry.[74] Equally, the fellow eyes of children with unilateral cataract have been shown to have normal sensitivity, even after being subjected to intensive occlusion therapy. Eyes affected by cataract were shown to have a restricted visual field, with restriction being more pronounced for longer durations of stimulus deprivation.[90]

2.6.1.1 Summary

There is currently little evidence to suggest that the fellow eyes of amblyopic subjects have a significant difference in visual field sensitivity compared to normal, binocularly developed visual systems, nor is there evidence currently to

support any adverse effects in terms of visual fields on better seeing eyes through the often intense occlusion therapy prescribed to children with cataract.

2.7 Disease processes affecting the visual field

A wide range of ocular, genetic and neurological disorders can affect the extent or sensitivity of the visual field. Each of these disorders has a distinct mechanism and is associated with a specific location in the eye or visual pathway. Thus, the resulting visual field defect can be localised at a particular site along the visual pathway as well as characterised according to extent/severity, making visual field assessment a valuable tool for diagnosis/management.

Inherited retinal diseases comprise the second largest group of blinding eye diseases in children. This heterogenous group of conditions are characterised by progressive loss of rod/cone function, making VF assessments a useful tool in monitoring disease progression.[91]

As well as these eye disorders, other processes can affect visual field sensitivity. Eyes treated for ROP with cryotherapy[92] or diode laser treatment[93] show slightly reduced peripheral field sensitivity, and this should be accounted for when assessing for other suspected causes of visual field loss. As discussed earlier, children with autism can have reduced sensitivity in their nasal fields, and children with sensori-neural hearing impairment have been shown to have reduced peripheral sensitivity compared to age-matched controls up to the age of 10 years.[94] However, adults with hearing impairment are known to have visual fields larger than age-matched controls, though the cause of this is not known.[95]

Incidences of a reduction in visual field sensitivity with vigabatrin use are well documented,[96-100] and all epileptic children managed with vigabatrin should undergo regular visual field assessments. This does prove challenging in young children or those with developmental delay, where formal perimetry is impossible. Current guidelines (published by the Royal College of Ophthalmologists, https://www.rcophth.ac.uk/standards-publications-research/clinical-guidelines/) suggest a developmental age of 9 years is "usually required to produce reliable perimetry."

Throughout the literature, it is highlighted that issues with perimetry are associated with individual disease processes. Thus, when designing a study investigating perimetry it is necessary to investigate different patient groups separately to ensure appropriate analysis and to be certain that no associations or characteristic defects are masked. The OPTIC study reported in this thesis investigated the role of perimetry in children with paediatric glaucoma and neuro-ophthalmic disease to address unanswered questions about perimetry in the management of these children, thus addressing gaps in the literature which contrasts with the extensive literature relating to adults.

A summary of relevant issues in relation to childhood glaucoma and paediatric neuro-ophthalmic disease is presented below, together with evidence relating to perimetry in children with these disorders.

2.7.1 Childhood glaucoma

Glaucoma is an optic neuropathy that causes retinal ganglion cell loss, followed by axonal loss in the optic nerve. The loss of these cells coincides with a loss of

function – i.e. visual field loss. In adults, glaucoma is the leading cause of irreversible blindness, affecting approximately 64.3 million people worldwide in 2013.[101] By contrast, the annual incidence of childhood glaucoma in Great Britain is 5.4 in 100,000 with a higher incidence in children of Pakistani origin (8.9 times higher) compared to Caucasians.[102]

Childhood glaucoma (comprising a group of distinct disorders) is a relatively rare, potentially blinding eye condition characterised by elevated intraocular pressure (IOP) and optic nerve damage. A full classification of the childhood glaucomas, both primary and secondary types, is reported in the literature.[103]

Primary congenital glaucoma accounts for most of the childhood glaucomas,[104] with aphakia/pseudophakia accounting for a large proportion of secondary glaucoma.[102] A review of the 10-year post-operative incidence of secondary glaucoma following cataract surgery in children, found an incidence between 10-25%,[105] underlying the need for prolonged follow-up in this group.

Primary glaucoma is most often managed surgically, and patients undergo lifelong follow-up to monitor progress. During this time, children are currently primarily monitored for changes in IOP and optic disc appearance. The stability of childhood glaucoma can also be inferred indirectly by assessment of changes in refractive error (myopic shift), corneal diameter and ocular volume, all of which can change in children with glaucoma. Importantly, assessment of visual fields is a key parameter in adults,[106] but because of the challenges in undertaking perimetry in young children, the technique is not yet widely used in the early years of disease management. Thus, there is presently very little literature in this area.

There are few studies looking at feasibility of testing and there is no literature on the use of common static visual field tests since the advent of shorter algorithms.[47] Static perimetry is the preferred method of assessment in glaucoma in adults as the central field is of particular interest and it does not require an experienced examiner to perform the assessment, and is therefore less resource intensive in a high volume setting.

One study of kinetic perimetry in children with congenital glaucoma found 50% of children aged 4-14 years with controlled IOP had visual field defects, with constriction of the I2e isopter being a significant feature (p=0.006).[107] The isopters V4e and I4e were reportedly comparable for patients and 'controls'. The localised field defects were similar to those seen in adult chronic open-angle glaucoma (nasal step/paracentral scotoma/arcuate scotoma), which have also been documented using static techniques.[108] One other study also noted a predilection for initial visual field damage in the arcuate area, followed by further arcuate and nasal loss.[109]

Semi-automated kinetic perimetry (SKP, Octopus 101) has been shown to be comparable to Goldmann visual fields in adults with visually significant glaucoma.[22, 110] There is evidence to suggest that in advanced adult glaucoma, the use of SKP yields better test/re-test reliability and 19/20 of the subjects in one study preferred performing a kinetic assessment.[111] There is no literature at present determining the use of SKP or its comparability to Goldmann visual fields in children with glaucoma.

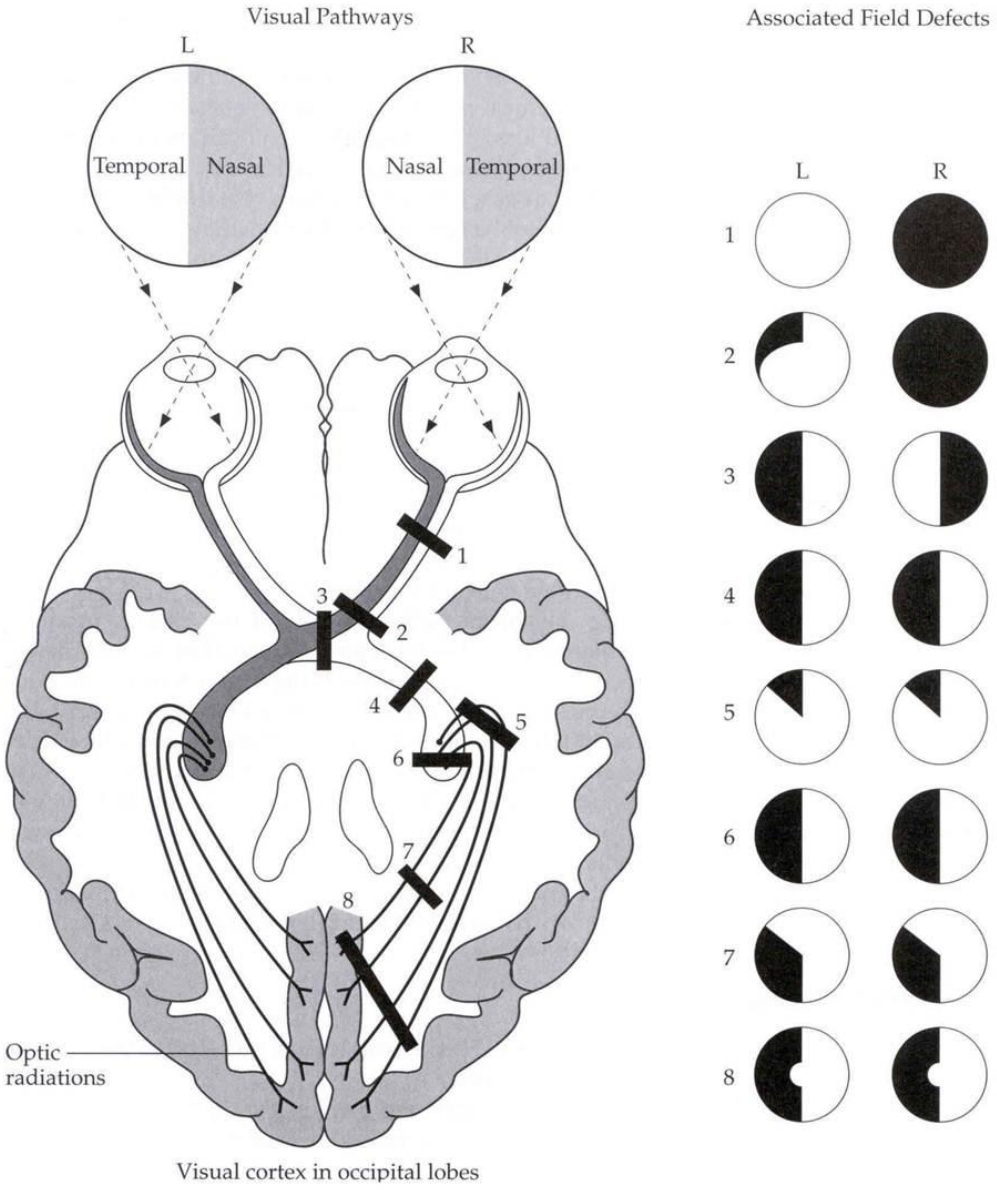
2.7.1.1 Summary

Currently, it is unclear how best to use perimetry in the management of childhood glaucoma. The most recent expert consensus statement from the World Glaucoma Association (WGA) states that perimetry "is worth introducing at that age [7-8 years] even if the initial results are unreliable."[112] There is however no stated guidance on which technique to employ or how to rate test reliability. Thus there is a need for research investigating the role of perimetry in these children.

2.7.2 Neuro-ophthalmic disease

There is a wide range of neurological conditions that affect children and which also impact upon the visual system and result in visual field abnormalities. Equally, there are disorders primarily/solely affecting the optic nerve which will also give rise to field defects. These defects can cause highly specific changes to visual field shape, and as such, kinetic perimetry is commonly used to monitor visual fields in these cases where changes occur outside the central 30° field.

Figure 9 (below) demonstrates the effects on the visual field caused by lesions at varying locations along the visual pathway. If the lesion lies on the visual pathway after passing the photoreceptor cells, it is classed as a 'neuro-ophthalmic' defect. These can affect either one or both fields.



www.studyblue.com

Neurological visual field defects:

1. *Total loss of the ipsilateral eye*	***5.*** *Junctional scotoma ("pie in the sky")*
2. *Total loss of the ipsilateral eye with an incomplete superior quadrantinopia*	***6.*** *Homonymous hemianopia*
3. *Bitemporal hemianopia*	***7.*** *Incomplete homonymous hemianopia*
4. *Homonymous hemianopia*	***8****. Homonymous hemianopia with macular sparing*

Figure 9. The visual pathway

2.7.2.1 Current clinical guidance

The Royal College of Paediatrics and Child Health (RCPCH) has endorsed guidelines for children with cancer – "Pathways to Diagnosis: The Diagnosis of Brain Tumours. " (developed by 'Headsmart', available from: http://www.rcpch.ac.uk/child-health/standards-care/clinical-guidelines-and-standards/endorsed-and-supported/oncology/guidel). This guidance was developed from a meta-analysis of 74 studies (*n* children = 4171, from a potential of 5620 papers), followed by a Delphi consensus procedure to develop guidelines based upon the evidence from these studies. The meta-analysis reported visual symptoms at presentation (depending on patient age and tumour location) in 7% to 41% of children. Between 5% and 8% had reduced visual fields at diagnosis. Recommendations from the report stated that neuro-imaging should be performed within 4 weeks if a child demonstrates 'a VF reduction.' The method of measuring visual fields, age at testing, and extent of visual field loss considered to be clinically significant were not reported.

2.7.2.2 Perimetric evidence

When selecting a perimetric test, a clinician has to be mindful of the strengths/weaknesses of each test modality and individual perimeters/algorithms within these. Studies have demonstrated that kinetic perimetry is preferable for monitoring neurological field defects and the effects of ptosis.[113, 114]

There are published guidelines on grading the extent of kinetic visual field defects in adults[115] as summarised in Table 3 (below). There are no comparable guidelines

for young children or guidance on the appropriateness of using an adult grading scale for children.

Table 3. Classification of neurological visual field loss

Goldmann perimetry

A. Grade 0. Normal visual field

B. Grade 1. Minimal visual loss (unlikely to be noticed by the patient)

1. Isopter constriction

step defects present that are less than 10° but greater than 5° in diameter

2. Defects not involving fixation

(a) relative scotomas that do not involve fixation

(1) up to 20°x20° in area outside 30°

(2) up to 10° in area inside 30°

(b) blind spot enlargement—involves central 10° but not fixation

3. Defects involving fixation: none—acuity is 20/20 or better

C. Grade 2. Mild visual field loss (may be noticed by patient—usually compromises function)

1. Isopter constriction

(a) up to 20° in area

(b) I4e isopter inside 30° nasally, 50° temporally

(c) I2e isopter inside 20°

2. Defects not involving fixation

(a) relative: less than one quadrant in size, defect greater than criteria of I.B.2.a

(b) absolute: less than 20°x20° in area

3. Defects involving fixation: acuity 20/30 or better

D. Grade 3. Moderate visual field loss (nearly always noticed by patient—interferes with function)

1. Isopter constriction

(a) greater than 20° to any isopter but more than 50° of field to the V4e stimulus

(b) I3e isopter inside blind spot

(c) I2e isopter inside 10°

2. Defects not involving fixation

(a) relative: greater than one quadrant but less than one hemifield

(b) absolute: greater than 20°x20° in diameter but less than one quadrant

3. Defects involving fixation—acuity greater than 20/30 but less than 20/100

E. Grade 4. Marked visual field loss

1. Constriction—less than 50° but greater than 20° in diameter to V4e

2. Defects not involving fixation

(a) relative: one hemifield or greater with more than 20° of field left to V4e stimulus

(b) absolute: greater than one quadrant with more than 20° to V4e stimulus

3. Defects involving fixation—acuity 20/100 to 20/200

F. Grade 5. Blinding visual field loss

1. Constriction—less than 20° to V4e

2. Acuity worse than 20/200

(Wall and George, 1991)

Neuro-ophthalmic conditions in adults are commonly diagnosed[116] and monitored using visual fields.[117] There is a less extensive literature base on perimetry in paediatric neuro-ophthalmology, but it is recognised that clinical conditions such as optic neuritis,[118] shunt-treated hydrocephalus,[119] craniosynostosis[120, 121] and optic nerve glioma in childhood can result in visual field loss. Pre-operative Goldmann visual fields have been shown to be a useful prognostic indicator for post-operative visual acuity, visual field sensitivity and tumour recurrence in children undergoing surgery for craniopharyngioma.[122] One study[123] reported on the utility of monitoring various ophthalmological measures (i.e. visual acuity, fundoscopy, ocular motility, nystagmus and visual fields) in the management of paediatric brain neoplasms and highlighted the importance of visual field testing in these children, particularly when monitoring for tumour recurrence.

A series of 92 children (aged 0-18 years), diagnosed with primary brain tumours of the central nervous system, most commonly pilocytic astrocytoma and medulloblastoma, but excluding those with optic glioma, craniopharyngioma, neurofibromatosis, or with existing known visual field defects were examined to look at the frequency of undiagnosed visual field loss. 15.2% (14/92) of all children were found to have visual field defects that had not previously been noted, as there was no clinical or symptomatic reason to suggest an abnormality, despite the fact that some of these children had hemianopic and quadrantanopic defects.[124] This highlights the value and importance of ophthalmological assessment and visual field testing in children with neurological disease.

A comparison of static perimetry to the gold-standard kinetic assessment in neurological conditions in adults has found that they are highly comparable. However, common static assessments cannot assess for residual islands of visual field function outside of 30° eccentricity.[125] It has been noted in adults with optic nerve head disease that static and kinetic perimetry can divulge complementary information, so both should be performed where possible.[126] In young children, the burden of performing both types of perimetry may be too great, so clarity about the relative benefits of each test modality is important.

One study comparing VEPs and visual fields in children/young people with optic nerve glioma found that only 15/40 (37.5%) aged 8-20 years could complete visual field testing, whereas all 40 (100%) of their subjects could complete VEP testing,[127] reflecting that VEPs require a substantially different degree of co-operation and no explicit recognition responses. As discussed earlier, VEPs play an important role in the diagnosis and management of a variety of conditions affecting eyes and vision. However, the results are not always directly comparable to visual field testing.

2.7.2.3 Summary

There is a paucity of robust data on perimetric techniques in childhood neuro-ophthalmic disease. The current clinical 'gold-standard' approach, kinetic perimetry using a Goldmann perimeter, is under threat as these perimeters are no longer commercially available. There is no evidence to recommend an alternative perimeter for this group of children. Further research is required to assess the

feasibility and reliability of new techniques/approaches against the current gold-standard.

2.8 Summary

Whilst there have been a number of investigations of perimetry in children, they most often focus on assessing the utility of individual test strategies. There are very few papers comparing visual field test strategies and, where they exist, these have small sample sizes, and often involve testing of older children. Analysis of visual field data often lacks objectivity, and the variety of methods used make comparisons between studies difficult.

There is a need for further investigation of the role of perimetry in the diagnosis and management of childhood eye disease. Specifically, investigations are needed to address the feasibility and reliability of perimetry in children across the age spectrum and to establish normative data for commonly used/accessible perimeters. Further to this, investigations examining children with specific ophthalmic conditions are needed, which would inform guidance of optimal approaches to perimetry in children e.g. with glaucoma and neuro-ophthalmic diseases, in whom the ability to perform robust and informative assessments of the visual field would prove particularly valuable.

Chapter 3 Study aims

The overall aim of the OPTIC study is to investigate the role of perimetry in the diagnosis and management of paediatric eye disease and develop optimal perimetric testing strategies for specific conditions.

The specific research questions are:

1.
    a. How feasible is visual field testing in children?
    b. How can reliability of visual fields be assessed?
    c. How reliable is visual field testing in children?

2.
    a. What is a normal visual field for a child (of a given age) without ophthalmic disease?
    b. What, if any, are the developmental changes in the visual field?

3.
    a. What is the optimal method of assessment for perimetric testing in children with glaucoma?
    b. What is the optimal method of assessment for perimetric testing in children with glaucoma?
        i. Is there a suitable alternative for the current gold-standard Goldmann kinetic perimeter in children?

Ultimately, based on the findings from this study, it is intended that clinical guidance will be developed relating to the assessment of visual fields in children with glaucoma and neuro-ophthalmic disease.

3.1 Study design

A prospective, interventional clinico-epidemiological study comparing different approaches to perimetry in three groups of children: control, glaucoma and neuro-ophthalmic. Table 4 (below, pg. 58) sets out the study design.

Table 4. Study Design

Aims	Subjects and Procedure
1a+b. To investigate feasibility, reliability, repeatability and acceptability of automated static perimetry (Humphrey), kinetic perimetry (Goldmann) and kinetic and static perimetry (Octopus) in **all children (those with and without ophthalmic disease).**	**Subjects – Groups A, B and C (see below)** Utilising data collected on: • Duration of assessment • Examiner report of test quality - Details on comprehension of instructions, fixation, fatigue, reaction times, behaviour, head positioning • Patient reported ease/difficulty of testing • Modifications necessary to complete assessment
2a+b. To report **normative data** for automated static, semi-automated kinetic, and manual kinetic perimetry drawing on **children without ophthalmic disease.**	**Subjects – Group A** Children without known visual field (VF) defects aged 5-15 years (patients with no VF defects / siblings of patients). **Procedures** Humphrey SITA 24-2 FAST, Goldmann kinetic, and Octopus kinetic assessment in one eye. Repeat measures at a follow-up visit to inform reliability/repeatability.

3a. To examine the value of static perimetry using the Octopus compared to the existing practices of using static perimetry using the Humphrey **in children with glaucoma.** **i) Comparison of Humphrey and Octopus static perimetry; to inform clinical monitoring of children.** **ii) Investigate the potential use of a combined kinetic/static Octopus programme in this patient group. Is anything additional achieved by full field VF testing in this patient group?** **iii) Comparison of SITA standard and FAST algorithms; to inform clinical monitoring of children**	**Subjects – Group B** Patients with glaucoma (may have had previous VF test)* **Procedures** **i)** Bilateral Humphrey SITA 24-2 FAST and combined static/kinetic Octopus in both eyes. **ii)** Follow-up visit will assess the comparability between SITA 24-2 FAST and SITA 24-2 standard algorithms in one eye only (affected eye of unilateral glaucoma or eye with most glaucomatous damage in bilateral glaucoma).
3b. To determine the value (strengths and weaknesses; extent of misclassification) of kinetic perimetry (Goldmann and Octopus) versus static perimetry (Humphrey) **in children with neuro-ophthalmic disease.** **i)** Comparison of Goldmann and Octopus kinetic perimetry; to inform future clinical monitoring of children if/when Octopus replaces Goldmann as perimeter of choice	**Subjects – Group C** Patients with neuro-ophthalmic disease (already had bilateral Goldmann; routine practice).

in paediatric populations. **ii)** Comparison of Goldmann kinetic and Humphrey static; to give guidance on appropriate perimetry for use in this patient group.	**Procedure** Bilateral kinetic Octopus with a bilateral static Humphrey at their follow-up visit.

**NB. A note will be made of previous VF testing on all patients. It is possible that some newly referred patients will have had previous VF testing elsewhere.*

The study design was developed to answer the research questions described above, whilst minimising the number of tests performed and repeat hospital visits required. This design allows the direct comparison of three visual field tests in a group of young children, whilst mitigating the effects of fatigue and improving the chance of recruitment into the study. To assess repeatability of visual field assessments, it would have been ideal to conduct multiple repeat tests over a short period of time. However, it is very difficult to recruit children to a study with this design. Therefore, the study was limited to one follow-up visit, which still allowed for collection of useful information to inform on the repeatability of visual field testing in children.

3.2 Ethics

The study was approved by the 'London – Bloomsbury' Research Ethics Committee (REC) (previously Great Ormond Street and Institute of Child Health Research Ethics Committee then Central London REC 2, Ref: 10/H0713/21).

The study was also listed on the NIHR portfolio, and participant accruals were updated monthly.

Chapter 4 Methods

To address the research questions posed in Chapter 3, children with specific ophthalmic characteristics were recruited from clinics at Moorfields Eye Hospital (MEH) and Great Ormond Street Hospital (GOSH) (see Chapter 3, Table 4, pg. 58). Children from all 3 cohorts undertook perimetry in a manner appropriate for their age. Generic methods are described below with methods specific to individual phases reported subsequently.

4.1 Generic test protocols

4.1.1 Recruitment

For each phase of the study, clinical case notes were examined by the PhD student (DEP) to identify potential participants. Participants and their parents were approached during their clinical visit and given written information sheets (Appendix III - Participant information sheets, pg. 188) as well as a short verbal explanation of the study. They were given time to read the information sheets and offered an opportunity to ask questions. Participants could be tested on the same day, or scheduled to return at a time that was convenient, either at a time during school holidays, or to coincide with their next scheduled clinic appointment.

A record was kept of those who did not wish to participate or could not, due to other constraints, in order to examine potential selection bias. Those who had not made a firm decision about participating and chose not to participate at the initial point of contact and subsequently could not be contacted were classified as 'non-responders'.

Prior to obtaining written consent, parents and participants were given a further opportunity to ask questions after being shown the testing room and perimeters. It was made clear to the children and their parents that their participation was voluntary and they did not have to take part if they did not wish to. They were also informed that they could ask questions at any time, or stop with testing (withdraw from the study) if they did not wish to continue. Parents were then asked to give written consent (Appendix IV - Parental consent form, pg. 219), whilst children gave verbal assent.

4.1.2 Pre-test procedures

All participants were assigned a unique study identifier. Study ID numbers were assigned sequentially, and all variables to be randomised were assigned numerical values (see Appendix V – Sample of test order randomisation, pg. 220). A sequence of random numbers was then generated and fixed in Microsoft Excel 2010®. Each number generated was independent of the previous, so that the chance of selection was not dependent on a previous value.

Data were extracted from clinical case notes about visual acuity, refractive error and clinical diagnosis.

Participants ability to perform testing was rated on each perimetric assessment using an Examiner Based Assessment of Reliability (EBAR) scoring system developed for this study (Table 5, below). The EBAR score is a qualitative, categorical system with outcomes of 'good', 'fair' or 'poor' quality of perimetric test and is independent of visual field outcome. The EBAR rating was designed for

this study and implemented to guide the evaluation of reliability in paediatric perimetry. Participants were assigned a score using the criteria below (Table 5).

Table 5. EBAR scoring system of visual field test quality

'Good' rating: Compliance with testing is good. The subject is able to ***maintain good central fixation*** and ***respond promptly***. They may have ***some fixation losses*** at times, but are able to understand and comply well with test instructions. General behaviour allows a ***comprehensive assessment.*** Overall, visual field outcome is expected to represent true visual field size/sensitivity.
'Fair' rating: Compliance with testing is mostly good. The subject ***may have moderate fixation losses*** with ***some variability in responses***. They are able to understand test instructions and their general behaviour allows for ***moderate co-operation***. They may show evidence of fatigue that affects performance and respond to the noise of stimulus presentation at times. Overall, visual field outcome is expected to be able to detect gross defects, but may over/under-estimate true visual field size/sensitivity.
'Poor' rating: Compliance with testing is poor. The subject demonstrates ***very high fixation losses or searching for stimuli***. They may be unable to ignore the sound of stimulus presentation and will therefore produce high false positive responses. They may also demonstrate ***highly variable responses***, with a possible lack of understanding of test instructions. Overall, test performance is not expected to represent true visual field size/sensitivity and will be ***unable to rule-in or rule-out visual field defects***.

For each subject a note was also made of any modifications required to complete each assessment. This included the use of an additional chinrest, or the need for rest breaks during the assessment. Data were collected on the length of each perimetric assessment to inform consideration of feasibility of assessments. Subjects who found it difficult to keep their chin resting at the perimeter were aided in keeping their heads in position. For Humphrey and Octopus perimetry,

the examiner was able to physically support a child's head, whereas for Goldmann perimetry, only verbal reminders were possible. A note was made of this, but it did not impact on EBAR rating unless associated with other factors (e.g. poor concentration).

4.1.3 Test procedure

4.1.3.1 Preparation of subjects

At the start of the assessment, the participant sat on a height adjustable chair and had the non-tested eye occluded with a soft eye pad. The subject was shown the relevant perimeter prior to testing and was given an explanation of the test procedure. This involved instructions to fix centrally and press their buzzer every time a light was perceived (either a flash or moving light dependent on the perimeter). He/she was also given an opportunity to test the buzzer. All instructions were delivered in age appropriate language. The child was then set up at the perimeter and seat and chin rest adjustments were made until the position was correct and the child felt comfortable. Additional padding on the chinrest to reach the correct height was given to any participant requiring it. Significant refractive errors were corrected using large aperture lenses for the I2e stimulus and static perimetry only using criterion modified from Henson[15]: ≥ +3.00 dioptre spheres (DS), ≥ -1.00DS, > ±1.00 dioptre cylinders (DC). The time taken to prepare the participant was recorded and a note was made of any modifications necessary to perform the assessment.

4.1.4 Testing

Encouragement and repetition of instructions were given throughout the tests. Participants were offered a rest break during the test if they appeared to be getting tired/losing concentration and if taken, this was recorded by the examiner.

4.1.5 Kinetic visual field assessments

Both the Goldmann and Octopus kinetic perimetry assessments were performed using the same testing protocol adapted from Werner.[14] Participants were prepared at the perimeter as described above. They were then shown the first test stimulus and were given three practice presentations to familiarise them with the task. Participants were informed when the practice finished and then commenced the test. Practice points were not used to form the test isopter.

Testing started with the largest/brightest stimulus i.e. assessing the far-peripheral first. The subsequent isopter was assessed with a smaller/less intense stimulus. Targets were presented along 12 cardinal meridia (every 30°), centripetally from a non-seeing area (Figure 10, below). Test points were started at a manually plotted location on the Octopus, with an automated speed of 5°/sec.

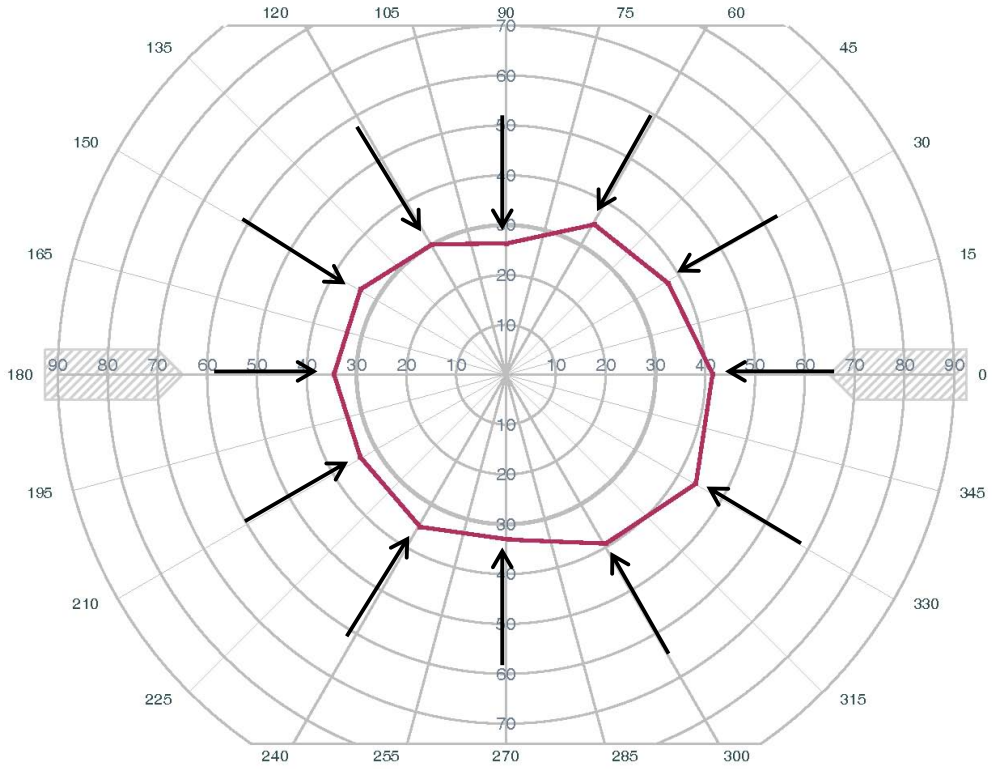


Figure 10. Kinetic perimetry – Centripetal presentation along 12 cardinal meridia

After plotting the 12 cardinal points, additional points were tested, in a non-randomised order along meridians 15° adjacent to the cardinal points starting with temporal field locations. This effectively 'filled-in' areas with larger distances between test points first, and allowed for more accurate plotting of visual field shape, up to a maximum of 24 points per isopter, for those children that could tolerate more extensive testing (Figure 11, below).

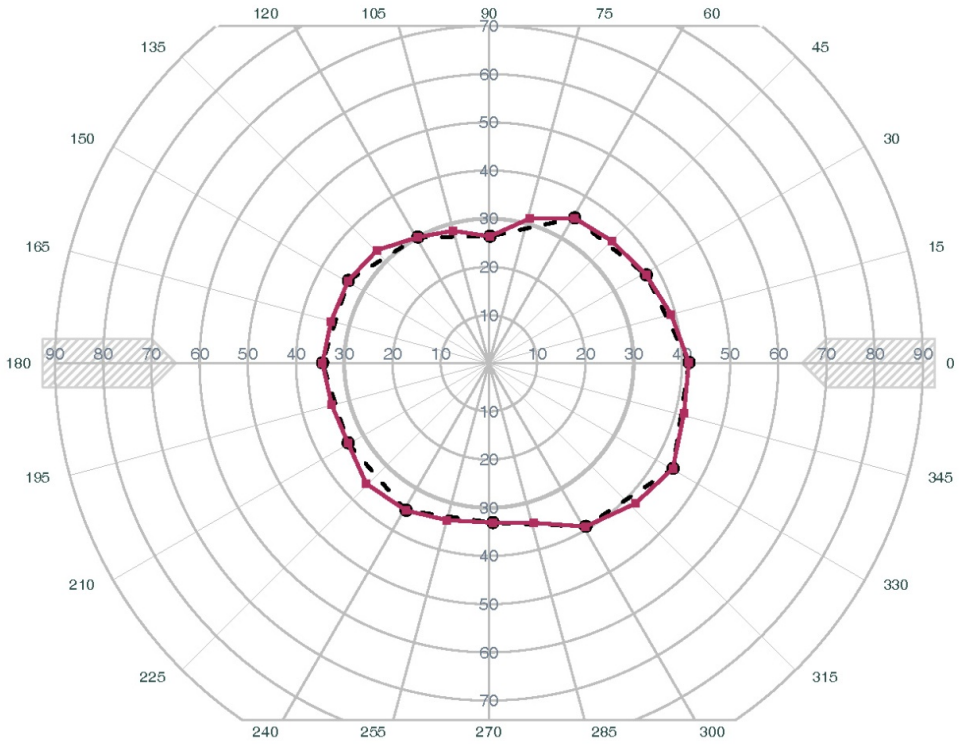


Figure 11. Formation of an isopter using 12 (black dashed line) vs. 24 points

Following this, an assessment of blind spot size/location was made. Static stimuli were presented to likely locations within the blind spot (approximately 15° into the temporal field and 3° below the horizontal midline), until an area without sensitivity was found. Eight kinetic stimuli were then presented outwardly from this point, until detected (Figure 12, below). The points were then joined to delineate the blind spot.

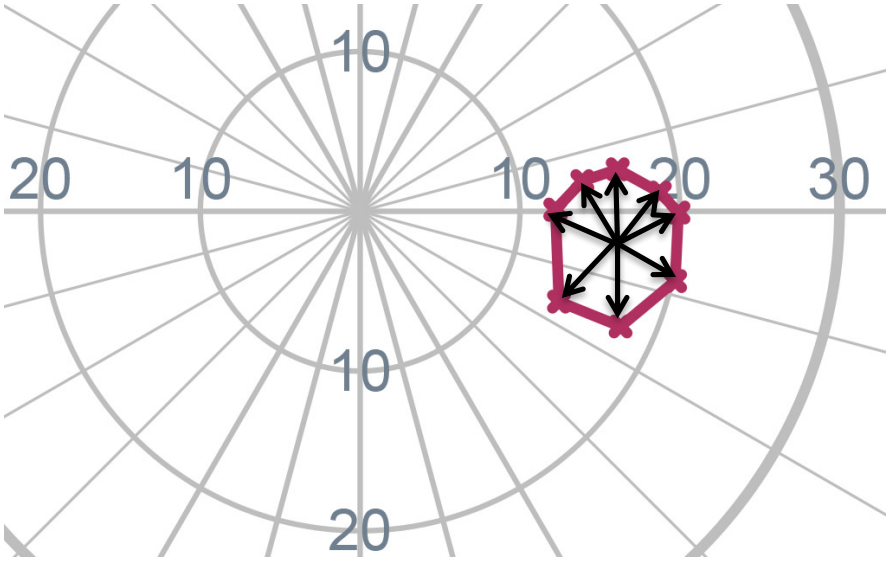


Figure 12. Plotting the blind spot using kinetic perimetry

4.1.6 The Kinetic Perimetry Reliability Measure (KPRM)

As reported earlier, there are no methods reported in the literature for assessing the reliability of a kinetic visual field. Examiner comments on quality are a useful tool, but these are not always easy to quantify, and quantifying reliability of visual field measurements is particularly important when monitoring for progression and reviewing visual fields that have been measured over an extended period.

To address this we devised a new measure, KPRM (Kinetic Perimetry Reliability Measure), for this study and piloted this technique using Goldmann perimetry. KPRM involves plotting four final points at the very end of an assessment using the outer isopter stimulus. One point was plotted in each quadrant along a randomly selected meridian (that had been used for plotting the original isopter). Comparing the distance (in degrees) between these four points and the point previously plotted on the outer isopter line (Figure 13, below) serves as a fast, visual representation of subject reliability. Taking a median value of the distance (in degrees) between these four KPRM points and the corresponding points gives

a KPRM score. Subjects were not allowed to repeat KPRM points if they lost concentration during this phase of the test. The effectiveness of this new measure was assessed and is reported later in this thesis.

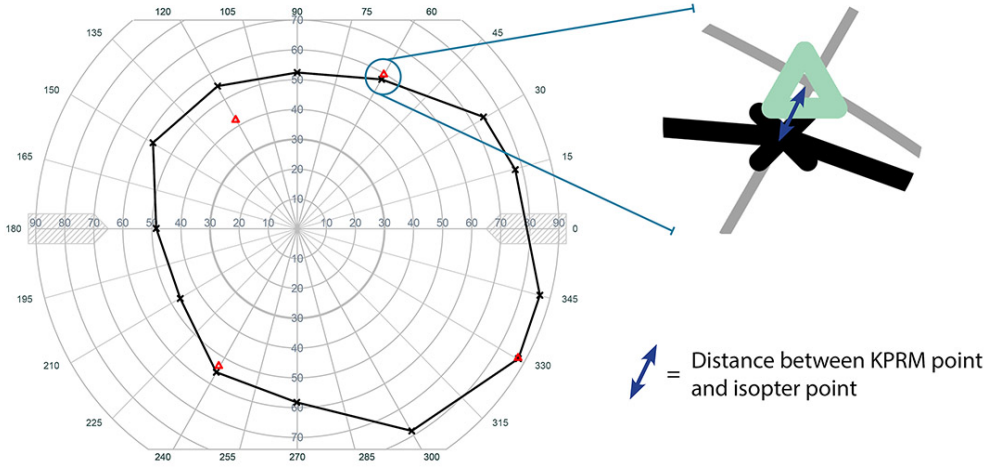


Figure 13. KPRM points (triangles) and an example distance (arrow) between a KPRM and corresponding point (cross)

4.1.7 Assessment of subjective experience of perimetry

After completing all of the perimetric assessments in a session, participants were asked questions about how difficult they found *each* assessment, scored on a 5-point Likert scale ranging from 'Very Hard' to 'Very Easy'. They were also asked if they had any other comments. These were recorded verbatim by the examiner. Thus, information on subjective experience was captured for every test.

4.2 Normative group (Group A)

4.2.1 Study population

Participants were recruited from patients attending Moorfields Eye Hospital, which lies towards the east of central London. It is a tertiary referral centre that accepts patients from school screening and other local sources.

Recruited children were primarily seen at the hospital for various eye disorders that do not impact on visual fields. They were therefore more accustomed to a clinical setting where they have to perform unfamiliar tasks for strangers than children in the general population, though none had any prior experience of perimetry. This study sample therefore reflects the patient population that might require visual field testing as part of clinical care and the demographics of the local area, with some subjects travelling from further away.

4.2.2 Identification and recruitment of subjects

Between May 2012 and November 2013, participants were recruited from general paediatric and strabismus clinics at MEH, where opportunities are greater (than at GOSH) for recruitment of children without ophthalmic disease that impacts on the visual field. Table 6 (below) lists inclusion/exclusion criteria for children in Group A.

Table 6. Group A inclusion/exclusion criteria

Inclusion Criteria
Children aged 5 to 15 years
No history of ophthalmological disease that could cause a visual field defect, but including children with refractive error, unilateral amblyopia and strabismus, where the fellow (normal) eye was to be tested
Visual acuity of 0.200 LogMAR (6/9.5 Snellen equivalent) or better in at least one eye
Exclusion Criteria
Children with any impairments, such as severe learning disability, which would make co-operation with formal perimetry impossible
Children not accompanied by a parent or legal guardian

4.2.3 Perimeters

Assessments were performed using an Octopus 900 (Haag-Streit AG, Switzerland), a Humphrey Visual Field Analyzer 750i (Carl Zeiss Meditec VG mbH, Germany) and a Goldmann perimeter (Haag-Streit, Bern, Switzerland). All tests were carried out by the PhD student (DEP) in the same visual field testing room (fitted with a blackout blind).

4.2.4 Test Procedure

For those with good acuity in each eye, and no strabismus/treated amblyopia, one eye was randomly selected and tested. In children with a better seeing eye, this (non-amblyopic) eye was selected for testing.

Subjects performed three visual field tests (Figure 14 (below)) and EBAR ratings were recorded for each test.

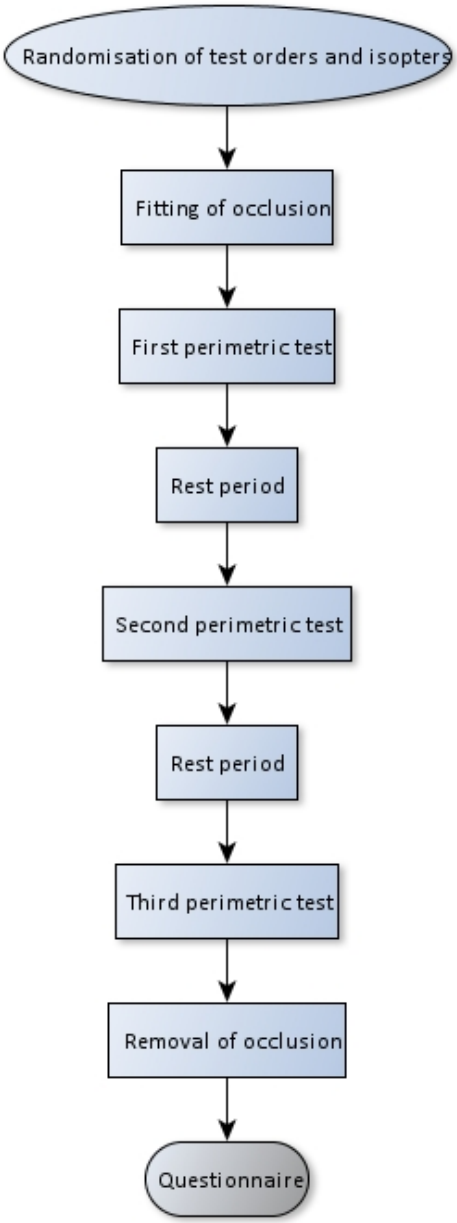


Figure 14. Group A - Test procedure overview

4.2.5 Kinetic visual field assessments

Both the Goldmann and Octopus kinetic perimetry assessments were performed using the same testing protocol (described above). Two isopters were plotted, the choice being randomised between III4e, I4e and I2e.

Participants were asked to "sit back and relax" between isopters, allowing for a very short rest (generally less than 20 seconds). During this period they were

shown the next test stimulus and then re-positioned to continue with the assessment.

The test procedure started with plotting an outer isopter, followed by inner isopter and then finally the plotting of the blind spot, with the I2e stimulus (stimulus speed of 2°/sec). This allowed children to get accustomed to testing using an easier stimulus, and allowed children to relate to an increased difficulty between isopters as "moving on to the next level."

KPRM points (pg. 67) were plotted after the blind spot plot and were only examined in Goldmann perimetry.

4.2.5.1 Achieving comparability between the Octopus and Goldmann perimeters

To allow comparison with the Octopus, the Goldmann targets were presented at approximately the same speed as Octopus targets and participants were given identical instructions. The test orders were randomised to minimise bias from learning effects from the first kinetic test.

Octopus readings for reaction times were not corrected as this function is not available on Goldmann perimetry and would alter the comparability of the two assessments.

4.2.6 Humphrey static perimetry assessment

Participants were assessed with the Humphrey perimeter using the SITA 24-2 FAST algorithm using the method described above.

4.2.7 Group A Follow-up visit test procedure

To assess repeatability of testing, a single repeat visit was conducted within 6 months of the initial visit, using exactly the same protocol, test stimuli and test order.

4.3 Glaucoma group (Group B)

4.3.1 Study population

Children with glaucoma meeting the inclusion/exclusion criteria as listed in Table 7.

Table 7. Group B inclusion/exclusion criteria

Inclusion Criteria
Children aged 5 to 15 years
Childhood glaucoma (all subtypes)
Visual acuity of better than 1.00 LogMAR (6/60) in at least one affected eye
Exclusion Criteria
Children with any impairments, such as severe learning disability, which would make co-operation with formal perimetry impossible
Children not accompanied by a parent or legal guardian

4.3.2 Identification and recruitment of subjects

Children were identified by examining medical records from specialist childhood glaucoma clinics at MEH and GOSH.

4.3.3 Perimeters

Assessments were performed using an Octopus 900 and a Humphrey Visual Field Analyzer. All tests were carried out by the PhD student (DEP).

4.3.4 Test procedure

Unless there was a clinical contra-indication, children were assessed by testing their right eye first, followed by their left eye. In children with only one seeing eye, only this eye was tested.

The SITA 24-2 FAST (Humphrey) was performed first, followed by a combined static/kinetic approach using the Octopus perimeter (Figure 15, below). Perimetric assessments were performed in the same order for each participant.

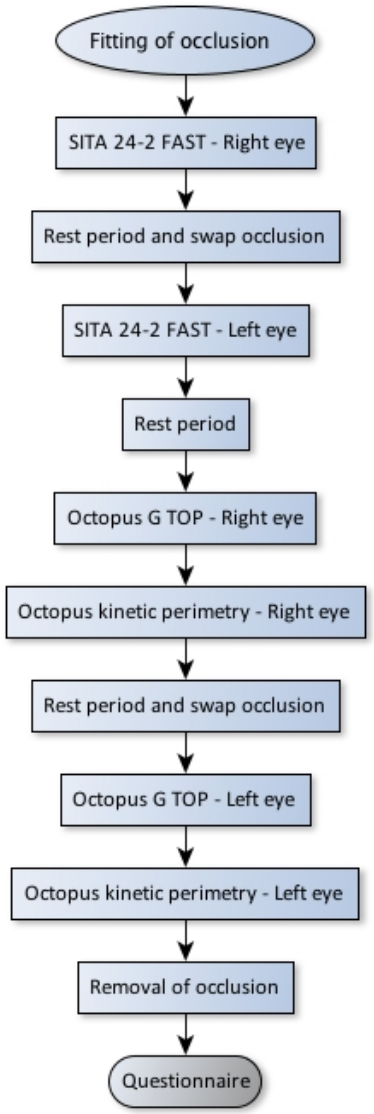


Figure 15. Group B - Test procedure overview – Initial visit

4.3.5 Static perimetry

Static perimetry was performed in the same manner as in the normative group (Methods – Humphrey static perimetry assessment, pg. 73) with gaze-tracking and blind spot monitoring attempted using the Heijl-Krakau method.

Participants were given a short rest break (generally between 1-2 minutes) between testing of each eye.

4.3.6 Combined static/kinetic perimetry

Children were assessed on the Octopus perimeter using the G-TOP static algorithm followed by one kinetic isopter. Refractive errors were corrected for the static algorithm only.

Kinetic perimetry was performed using either isopter V4e, III4e or I4e, dependant on the child's ability to see the stimulus. The isopter was plotted using the same method described in Chapter 4 (pg. 65), i.e. 12 initial points every 30°, followed by further points to delineate isopter shape, up to a maximum of 24 points.

4.3.7 Follow-up visit test procedure

Participants were invited back for a second visit, and the field of one eye was assessed with two perimetric tests. The eye with the most advanced glaucoma was selected, using the HFA 'SITA 24-2 FAST' and 'SITA 24-2 standard' algorithms, performed in a randomised order, unless that eye had an acuity too poor to assess visual fields (worse than 1.0 LogMAR). In these cases, the fellow eye (bilateral glaucoma only) was assessed. This allows for a direct comparison between the output, duration, and acceptability of the algorithms.

4.4 Neuro-ophthalmic group (Group C)

4.4.1 Study population

Children with confirmed neuro-ophthalmic disease meeting the inclusion/exclusion criteria as listed in Table 8 (below).

Table 8. Group C inclusion/exclusion criteria

Inclusion Criteria
Children aged 5 to 15 years
Confirmed neuro-ophthalmic disease
Visual acuity of better than 1.00 (6/60) in at least one affected eye
Exclusion Criteria
Children with any impairments, such as severe learning disability, which would make co-operation with formal perimetry impossible
Children not accompanied by a parent or legal guardian

Children were identified by examining medical records from ophthalmology clinics at GOSH.

4.4.2 Test procedure

Children performed Goldmann perimetry (as part of their routine care) followed by Octopus kinetic perimetry (after a short rest break). Perimetric assessments were performed in the same order for each participant.

Unless there was a clinical contraindication, right eyes were tested first, followed by left eyes. The testing procedure followed the same protocol used for Group A (summarised below, Figure 16), with a few key differences:

1. For children with hemianopia (Appendix II - Glossary of terms, pg. 185): Targets were presented centripetally for the seeing half of the field, but were presented horizontally, from non-seeing to seeing, every 15° along the y-axis for the non-seeing half of the field.

2. Target isopters were selected from previous Goldmann kinetic fields to ensure clinical comparability between tests. Identical isopters were used for the Octopus kinetic assessment to allow a direct comparison within subjects.

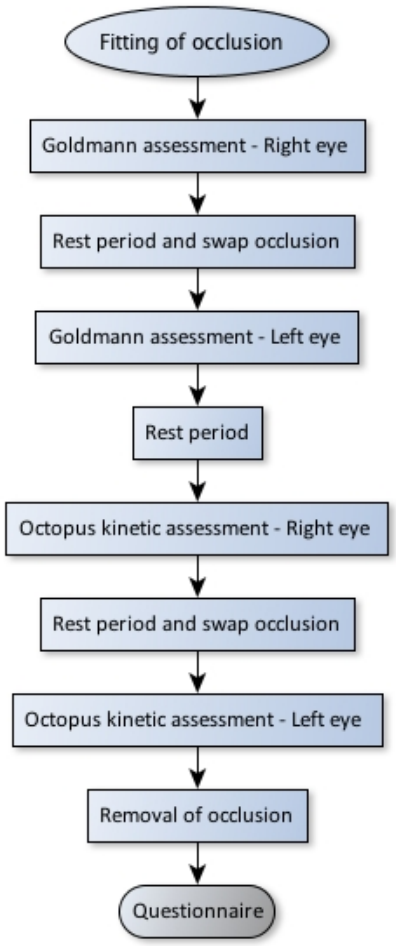


Figure 16. Group C - Test procedure overview – Initial visit

4.4.3 Follow-up visit test procedure

Participants were invited back for another study visit at which time they were assessed with a repeat Goldmann visual field test, followed by a bilateral Humphrey visual field test using the SITA 24-2 FAST strategy. The protocol otherwise remained identical to the first Group C visit.

4.5 Data management

4.5.1 Data

Data were recorded on paper data collection documents during the clinical assessments. This included details of the participants' clinical characteristics, visual field test results, questionnaire responses and examiner comments on reliability. Octopus raw data were extracted from the perimeter in a text string format (.txt files). XML and TIFF files of visual field test results were exported from the Humphrey Field Analyzer (HFA).

4.5.2 Data entry

Data from paper collection documents were entered into the database software REDCap[128] (Research Electronic Data Capture) hosted securely at UCL Institute of Child Health. The REDCap database was exported as a STATA (StataCorp. 2011. *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP) database file for analysis. Goldmann perimetry results were scanned and stored as JPEG files.

4.5.3 Data governance and security

All electronic files were kept on password-protected computers/servers and paper records were kept in a locked cabinet in a locked room. Three backup copies of all electronic files were kept in case of data corruption.

4.5.4 Data manipulation

4.5.4.1 Kinetic perimetry data

Scanned Goldmann visual fields were digitised using Engauge digitizer software (open-source, www.digitizer.sourceforge.net). Each visual field had independent axis points defined and then response points were extracted by isopter and exported to comma delimited (CSV) files.

Raw Octopus data were cleaned and ordered in R (The R Project for Statistical Computing (R v3.2.1, www.r-project.org)). The code developed by Prof. Mario Cortina Borja and DEP (UCL ICH, PPP) provides a framework for the analysis of kinetic perimetry data and has been published as the R package `'kineticF'`.[129] All code developed is listed in Appendix VI – `kineticF` code (pg. 221).

Following the digitisation of Goldmann data, and the cleaning of Octopus raw data, the two databases for each perimeter were arranged in an identical format, thus allowing identical analyses to be performed. Points were split into 24 sectors, representing responses every 15°. Distances from the origin (at the centre of the field) to these points were calculated allowing for isopter area calculations to be made. Left eye responses were flipped to mirror right eyes for analysis.

4.5.4.2 Automated static perimetry data

The electronic outputs from the HFA (XML and TIFF files) were 'read' by R using code developed at City University (personal communication: Richard Russell). By using this method it was possible to extract raw sensitivity values from HFA data, with no typographical errors. As with kinetic data, left eye responses were flipped to mirror right eye responses for analysis.

4.5.5 Data quality checks

To minimise errors in data management and analysis, a number of data quality checks were implemented, at various stages of data entry and analysis. The REDCap database was coded with automated checks, to stop values being omitted, or being inputted in an incorrect format at the data entry stage. Branching logic was used to ensure that relevant fields were populated and to reduce unnecessary fields being presented. After all data were digitised, they were imported into STATA for data checking. The data were examined for completeness and outliers were checked against the data collection forms to ensure transcription accuracy. Any errors/omissions were corrected using the source data. In a random sample of 5% of the datasets, double data entry was undertaken.

4.6 Statistical methods

4.6.1 Sample demographics (all groups)

Descriptive analyses of participation rates and participant demographics (including age, sex and ethnicity of both participants and non-participants) were performed. Barriers to participation were explored, providing insight into the design of future clinical research recruiting children with and without ophthalmic conditions.

4.6.2 Feasibility and reliability of perimetry (all groups)

Initial analysis involved a descriptive exploration of test feasibility and reliability. Test qualities (EBAR ratings) were reported as proportions per age group for each perimeter. Changes in quality with age were explored using multinomial logistic regression and comparisons between perimeters were assessed using chi-squared tests.

4.6.3 Subjective report of test difficulty (all groups)

Participant responses were recorded on a 5-point Likert scale. Comments made by children on the test procedure/difficulty were recorded and categorised into common themes. Comparisons between self-reported test difficulty and examiner rated test reliability (EBAR) were made.

4.6.4 Perimetric test repeatability (Group A)

Isopter area values for kinetic perimetry and Mean Deviation (MD) values for static perimetry were used in the assessment of test repeatability. The Bland-Altman method[130] was undertaken, examining agreement between initial and follow-up visits in participants with 'Good' quality EBAR ratings.

4.6.5 Generating normative data (Group A)

4.6.5.1 Kinetic perimetry data

Normative isopter areas were calculated using `kineticF`. The Octopus perimeter reports these as part of a test output. Thus, the normative ranges reported here provide clinically comparable values.

Linear regression of isopter area and age was undertaken to explore visual field development during childhood.

To model normative sensitivity lines (isopters) we fitted linear quantile mixed-effects regression models based on the asymmetric Laplace distribution.[131] These models can estimate fixed effects parameters of harmonic terms with arbitrary periods including interaction terms, and can include random effects terms reflecting unobserved within-subject variability. Quantile regression models can appropriately describe skewed and kurtotic distributions without making specific

distributional assumptions. These models can be considered distribution-free and estimate parameters from linear predictors defined on a set of fixed quantile values.

An example of the R code required to fit models in this class is shown in Table 9 (below, pg. 84 – developed with Prof. Cortina-Borja). The linear predictor in this model was chosen from among a family of possible harmonic functions by minimising the Bayesian Information Criterion (BIC).[132] We also included a random effect term on the intercept of all linear predictors considered with clusters based on the subject's identity. This model selection procedure led to fitting six fixed effects parameters corresponding to an intercept, and sine and cosine terms with periods 1 and 2, and an interaction term between the sine function with period 1 and the cosine function with period 2.[133]

Table 9. Fitting a linear quantile mixed-effects regression model to kinetic perimetry data

```
arcsX<-seq( 0, 2*pi, length=1000) ## sequence on a fine grid -  to
predict

arcsX<- data.frame(theta=arcsX)
arcsX<- unlist(arcsX)
c1<- cos(arcsX)
s1<- sin(arcsX) ## generate basic harmonic terms

library(lqmm)

## assumes package lqmm is available; otherwise use
## install.packages("lqmm") to load it before calling it

tau<- c(0.025, 0.5, 0.975) ## quantile values


mod3<- lqmm( r ~ cos(theta) + sin(theta) + cos(2*theta) +
sin(2*theta)
             + I(sin(theta)*cos(2*theta)), tau=tau,
             random= ~1, group=ID,  na.action=na.omit,
             data=test)

## An example of a linear mixed quantile regression model
## Random terms are defined only for the intercept
## Clusters are defined by subjects' IDs
## The linear predictor contains five harmonic terms in this case


pred3<- matrix(NA, ncol=length(tau), nrow=length(arcsX))
## reserve space for predictions

## prediction
for (i in 1:length(tau)) ## predict each quantile separately
  {
    beta<- mod3$theta_x
    pred3[,i] <- beta[1,i] + beta[2,i]*cos(arcsX) +
beta[3,i]*sin(arcsX) +
                 beta[4,i]*cos(2*arcsX) + beta[5,i]*sin(2*arcsX) +
                 beta[6,i]*sin(arcsX) * cos(2*arcsX)
  }


innerx<-  pred3[,1]*c1
innery<-  pred3[,1]*s1 ### project into polar coordinates

outerx<- pred3[,3]*c1
outery<- pred3[,3]*s1

inner<- cbind(innerx, innery)
outer<- cbind(outerx, outery)
```

```
inner<- rbind(inner, inner)
outer<- rbind(outer, outer)

x1<- c(outer[,1], rev(inner[,1]))
y1<- c(outer[,2], rev(inner[,2]))

## x1 and y1 are the polar co-ordinate values of predicted points
```

Bland-Altman plots were used to compare agreement in isopter areas between the two kinetic perimeters, informing clinical decisions regarding the interchangeability of techniques in long-term care.

4.6.5.2 Static perimetry data

Linear regression of MD with age was performed. As with kinetic perimetry, the data were plotted and explored to examine for visual field development and maturation.

Assuming maturation occurs between the age of 5 and 15 years, there would be an increase in MD towards 0 MD, the average mean deviation in adults. Therefore, the line of best fit of these data will not be a quadratic curve, as there is a natural asymptote. Fitting a 4-parameter logistic nonlinear regression model with an asymptote, age at change of inflection and 2 slope coefficients would allow for estimating this asymptote.

However, a piecewise regression model would firstly allow for estimating the age of inflection and secondly examination of the rate of change in mean deviation before and after this age point. By reporting the coefficient after the point of inflection, we can see if this differs from 0 i.e. have children over the point/age of inflection achieved adult levels of mean deviation? Thus, a piecewise regression model was fitted to Humphrey static MD data.

4.6.6 Analysis of glaucomatous VF defects (Group B)

The feasibility and reliability of static vs. combined static/kinetic perimetry was reported descriptively. Changes in automated reliability indices (RI's) with age were explored. The use of RI's was compared to EBAR to report on the potential for misclassification of reliability in clinical cases.

In children with unilateral glaucoma, analyses of VF function in 'unaffected eyes' provided information regarding the 'normality' of eyes in an affected visual system. If normal, these fellow eyes can serve as controls within subjects, tracking a child's visual development. Thus, the outputs (MD, isopter area) of unaffected eyes were compared to our normative (group A) data.

Knowledge of the extent of VF damage aids monitoring of disease progression. It is also useful in understanding how vision could affect daily/visual function. It is not known whether extent or nature of VF damage is directly associated with VA or IOP in children. Thus analyses were conducted modelling for associations between both MD and PSD/sLV, with VA, age and IOP to assess whether the latter variables can be used to infer VF damage in patients in whom VF testing is not possible.

Outputs from the Humphrey 24-2 SITA FAST algorithm were compared directly to Octopus G-TOP values. This was performed with an awareness of the differences in the test algorithms, perimeter/stimulus luminance and normative datasets from which test results are compared to generate MD and PSD/sLV values. Nevertheless, this comparison is useful in guiding clinical interpretations. Thus, MD values were correlated, and Bland-Altman plots used to report agreement

between values. PSD and sLV values were also compared using the Bland-Altman technique.

To examine the comparability of the kinetic and two static techniques in detecting VF defects, each visual field was graded using an existing classification system (devised by Aulhorn and Karmeyer[134]). This system classifies visual fields based on the type and extent of defect, regardless of perimeter/technique used (summarised in Table 10 (below)) and assumes that a full kinetic VF test has been performed. As the kinetic protocol used here involved assessment using only one far-peripheral isopter, those graded as stage II or III were combined for analysis of static vs. kinetic techniques.

Table 10. Classification of glaucomatous visual field defects

Stage 0	No visual field loss.
Stage I	Only relative defects.
Stage II	Spot-like, stroke-like, or arcuate absolute defects, having no connection to the blind spot.
Stage III	Arcuate absolute defects already connected to the blind spot, with or without a nasal break-through into the periphery.
Stage IV	Extensive ring-shaped or half ring-shaped defects, with a central island of sensitivity maintained.
Stage V	Central island collapse, with only the temporal visual field area remaining.

Other scoring systems[117, 118] such as the Advanced Glaucoma Intervention Study (AGIS),[135] Glaucoma Staging System (GSS)[136] and GSS2[137] were appraised but these are only validated for use with specific static algorithms, and were therefore not suitable for use here.

A comparison of the SITA standard and FAST algorithms was made, examining factors that affect the clinical choice of test procedure, such as test duration (linear regression), EBAR ratings (chi-squared), and test difficulty (descriptive). Output values (MD and PSD) were compared using the Bland-Altman technique.

Subjects' responses on experiences of testing were reported descriptively. Verbatim comments were categorised and strong themes/elements were reported to identify factors that children regard as important to the visual field assessment process.

4.6.7 Analysis of neuro-ophthalmic VF defects (Group C)

The feasibility and reliability of Goldmann and Octopus kinetic and Humphrey static perimetry was reported descriptively. EBAR ratings were compared to report on the potential for differences in test reliability between perimeters.

Kinetic fields were classified using the modified Wall and George system[120] shown below (Table 11). Results were compared to age-matched normative data generated by testing of children in group A (see Appendix – section 9.8.3, pg. 341) to determine whether children exhibited VF loss. Classification scores were then compared between perimeters.

Table 11. Classification of neuro-ophthalmic visual field defects

Grade 0	**Normal visual field**
Grade 1	**Minimal visual field loss** *Isopter constriction.* Step defects present that are less than 10° but greater than 5° in diameter. *Defects not involving fixation.* Relative scotomas up to 20°×20° in area outside 30°, or up to 10° in area inside 30°.
Grade 2	**Mild visual field loss** *Isopter constriction.* up to 20° in area, I4e isopter inside 30° nasally, 50° temporally I2e isopter inside 20° *Defects not involving fixation.* Relative – less than 1 quadrant in size, absolute – less than 20×20 in area
Grade 3	**Moderate visual field loss** *Isopter constriction.* Greater than 20° to any isopter but more than 50° of the field to the V4e target, I3e isopter inside the blind spot, I2e isopter inside 10°

	Defects not involving fixation. Relative – greater than 1 quadrant in size but less than one hemifield, absolute – greater than 20°×20° in diameter but less than one quadrant
Grade 4	**Marked visual field loss** *Isopter constriction.* Less than 50° but greater than 20° in diameter to V4e target *Defects not involving fixation.* One hemifield or greater with more than 20° in diameter to V4e, absolute – greater than one quadrant with more than 20° to V4e
Grade 5	**Blinding visual loss** Isopter constriction. Less than 20° to V4e

Visual field data from kinetic perimeters were analysed and compared directly using Bland-Altman analysis of isopter and blind spot area.

Subjects' responses on experiences of testing were reported descriptively and analysed using the same methods as children with glaucoma.

4.6.8 Summary

As described above, the OPTIC study developed and utilised new approaches for data access, management and analysis of visual field data. A plan of analysis was devised *a priori*, which involved baseline descriptive statistics, followed by fitting of regression models and other analytical methods to further explore associations between variables. Specifically, we aimed to investigate associations to explore:

- Feasibility of testing – i.e. which tests can be performed and completed? How does age affect this and the level of detail possible in a kinetic visual field assessment?

    - How long does it take to perform a perimetric test? Does this change with damaged visual fields?
    - Does the feasibility of testing change for children with glaucoma and neuro-ophthalmic disease?

- Reliability of testing – i.e. what proportion of tests in children are of an acceptable quality or reliability? How does this change with age? How can we rapidly, visually and quantitatively assess the reliability of kinetic visual fields?

    - Does the reliability of testing change with increasing visual field loss?
    - Does the child's perception of test difficulty relate to test quality?

- Repeatability of testing – i.e. how much variation is present between an initial and follow-up visual field test in children with normal visual fields?

- Normative visual field output – i.e. what is a normal visual field test result for a child? Does this change with age? If so, which parts of the visual field change the most?

The findings are reported in Chapter 5.

Chapter 5 Results

5.1 Normative group (Group A)

5.1.1 Sample demographics

One hundred and fifty-four participants (Figure 17, below) were tested between May 2012 and November 2013 from 348 eligible subjects (44.3%). Of these, 43 (27.9%) returned for a follow-up visit.

132/348 (37.9%) of those approached to take part in the first phase of the study (normative group) decided to not participate on the initial day of contact. When subsequent attempts to contact these families failed, they were categorised as 'non-responders', and constitute 68% (132/194) of the total non-participants.

The reasons given for declining to participate were predominantly due to time constraints, with parents/children unwilling or unable to take part in a study of this length. 23/34 (67.6%) stated this reason, with 11/34 (32.4%) stating they were not interested in taking part in the project/research (Figure 18, below).

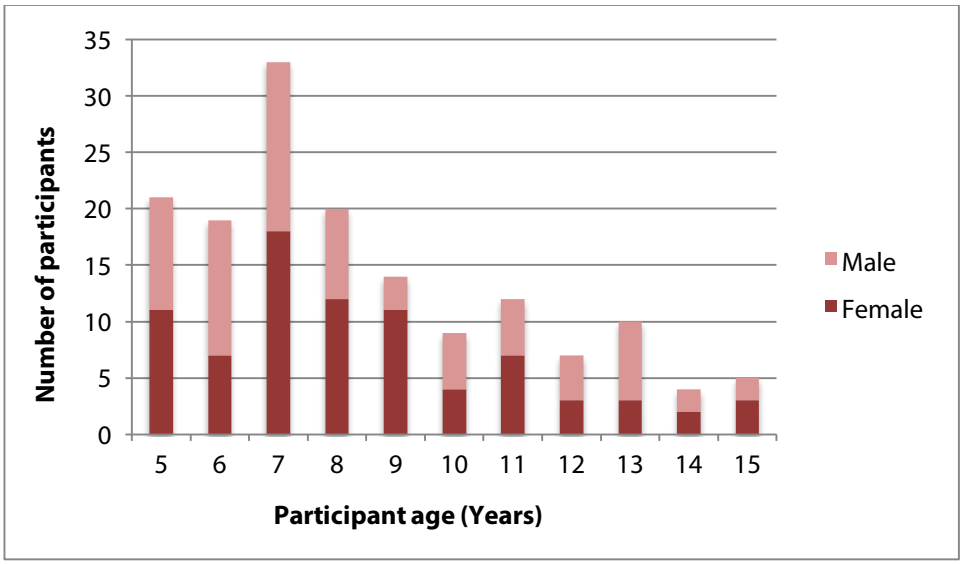


Figure 17. Group A - Sample demographics by age and sex (*n*=154)

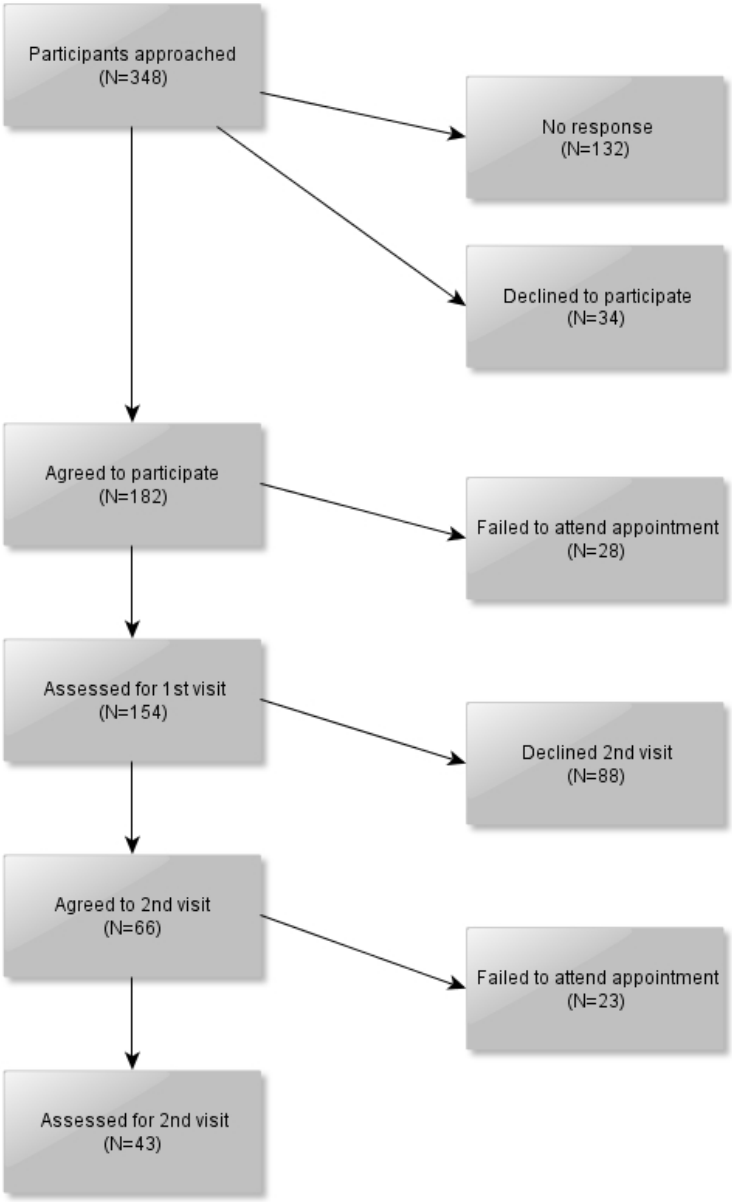


Figure 18. Sample breakdown for initial and follow-up visits

118/154 (76.6%) of the sample were White, with 9.7% Indian, 8.4% Black and 5.2% of mixed ethnicity. Those declining to participate were of similar age and ethnicity distribution to those participating.

Median refractive error was 0.00D (spherical equivalent) IQR= 0D to +2.5D, range = -10.00 to +6.75D. 56/154 (36.4%) participants had strabismus, and 35/154 (22.7%) had unilateral amblyopia.

5.1.2 Feasibility of perimetry in children

No child had to stop testing completely due to fatigue or an unwillingness to continue with the assessment. All three perimetric tests were feasible for all ages (Table 12, pg. 94).

Table 12. Participant demographics and test feasibility for all perimeters (*n*=154)

Age group (years)	Sex		Number (%) completing assessments			Mean test duration (min) (SD)		
	Male	*Female*	*Goldmann*	*Octopus*	*Humphrey*	*Goldmann*	*Octopus*	*Humphrey*
5-6	22	18	36 (90)	32 (80)	40 (100)	9.2 (1.9)	9.1 (1.4)	7 (1.3)
7-8	23	30	51 (96.2)	48 (90.6)	53 (100)	9.4 (1.8)	9.1 (1.8)	6.2 (1.0)
9-11	13	22	35 (100)	32 (91.4)	35 (100)	9.3 (1.3)	8.5 (1.0)	5 (1.0)
12-15	15	11	26 (100)	25 (96.2)	26 (100)	8.6 (1.1)	8 (0.9)	4.6 (0.7)

** Test duration values include preparation and assessment tasks*

For Octopus and Humphrey perimetry, 13/154 (8.4%) children, all under 8 years of age, required the use of additional chinrest support for correct positioning at the perimeter. Only 1/154 (0.7%) child required modifications to be successfully aligned for Goldmann perimetry (sat up on knees to reach the required height). Only 8/154 (5.2%) of all children showed visible signs of fatigue for Humphrey perimetry compared to 13/154 (8.4%) performing Goldmann and 19/154 (12.3%) performing Octopus assessments. No child above 9 years was affected by fatigue

for Goldmann and Humphrey perimetry. Only 1/154 (0.7%) child, aged 7 years, required a break during Goldmann perimetry, with 4 /154 (2.6%) and 9/154 (5.8%) requiring breaks for Octopus and Humphrey perimetry respectively.

Regression analysis was performed, modelling total test duration (including preparation tasks), EBAR rating, age and sex for each perimetric assessment. The duration of Goldmann perimetry was found to reduce with increasing test quality (p=0.021, for 'poor' to 'fair' quality, and p<0.001, for 'poor' to 'good' quality), such that tests of poor quality had a mean duration of 9.17 minutes (SD 1.94) and good quality tests took 6.82 minutes (SD 1.16). No effect of age (p=0.211) or sex (p=0.388) were noted.

Smaller effects were seen for Octopus perimetry test duration when compared to Goldmann perimetry. There was a slight reduction in test duration between 'poor' and 'good' tests (p=0.035) with poor tests having a mean duration of 7.18 minutes (SD = 2.01) and good tests having a mean duration of 6.29 minutes (SD = 1.24). No significant change was noted between 'poor' and 'fair' quality tests (p=0.474). A trend of reducing test duration with age was seen (p=0.030), unmodified by additional adjustment for sex (p=0.339) (see Table 12, pg. 94).

Finally, Humphrey perimetry results showed a clear trend for a reduction in test duration with increasing quality (p<0.001) and age (p<0.001). The mean test duration of a poor quality static field was 5.61 minutes (SD 1.38) compared to 3.69 minutes (SD 0.72) for good quality tests. No effects of sex were found (p=0.768).

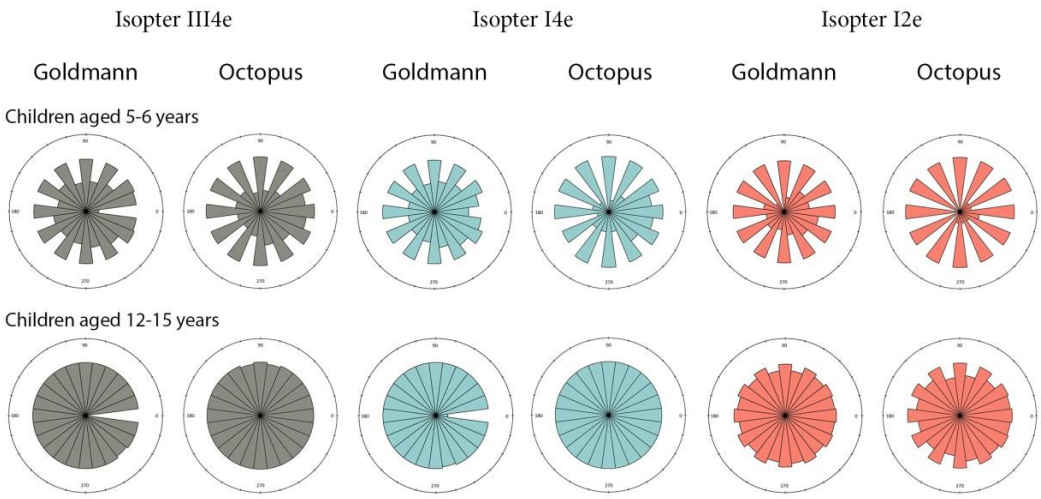


Figure 19. Rose diagrams of the frequency of points plotted along individual meridians for Goldmann and Octopus perimetry for children aged 5-6 years compared to 12-15 years

**The empty sectors at 0° for Goldmann perimetry isopters III4e and I4e correspond to the 'void' area in the perimeter bowl.*

For all isopters on both kinetic perimeters, there was a statistically significant increase in the number of points that could be plotted per isopter with age (p<0.0001) (Figure 19).

5.1.3 Reliability of perimetry in children

Figure 20 (below) demonstrates the change in the proportion of 'good' test quality (EBAR) ratings with age for each perimetric assessment. Only Goldmann perimetry had >50% of tests rated as 'good' in children aged 5-6 years but test reliability improved with age for all perimeters (p<0.0001). By ages 7-8 years there was a shift from large proportions of 'fair' tests to 'good' quality tests. In children over 9 years of age, no significant difference was found in the proportion of good quality tests between Goldmann and Humphrey assessments (χ^2, p=0.123).

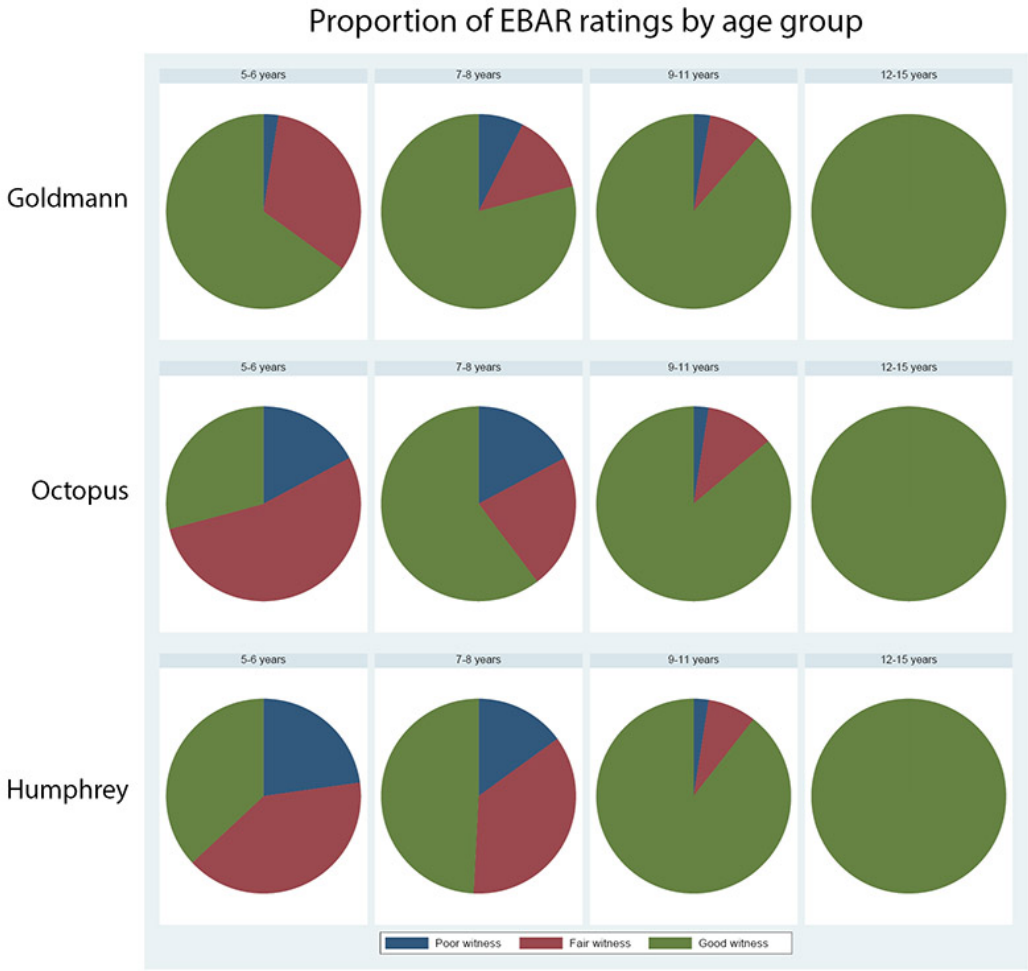


Figure 20. Distribution of quality ratings (EBAR) per perimeter, by age groups

Traditional reliability indices (RI) (fixation losses ≥ 25% or false positives ≥15%) indicated a large number of assessments (125/154 (81.2%)) would be classified as unreliable. Traditional RI's disagreed with EBAR in 74/154 cases (48.1%) (Table 13, pg. 98).

Table 13. Comparison of EBAR (test quality) ratings with automated reliability indices for Humphrey perimetry

EBAR Rating	False Positives		Fixation Losses		Traditional Reliability Indices	
	<15%	*≥15%*	*<25%*	*≥25%*	*Reliable*	*Unreliable*
Good	87	11	30	68	26	72
Fair	19	19	1	37	1	37
Poor	6	12	6	12	2	16
Total	112	42 (27%)	37	117 (76%)	29	125 (81%)

** Traditional reliability indices are defined here as fixation losses ≥ 25% or false positives ≥15%*

Splitting the two variables that compose the reliability index shows that fixation losses alone demonstrate poor agreement with EBAR (test for trend; p=0.196). However, only 42/154 (27%) assessments would be classified as unreliable using false positives alone and there is better agreement with EBAR, (test for trend; p<0.001), with only 17/154 (11%) assessments showing disagreement.

In 16/154 (10.4%) (Goldmann) and 45/154 (29.2%) (Octopus) children it was not possible to reliably plot the blind spot. Of these 10/16 (62.5%) and 23/45 (51.1%) had tests rated 'fair' or 'poor' quality for Goldmann and Octopus respectively.

5.1.3.1 The Kinetic Perimetry Reliability Measure (KPRM)

103 children with median age 8.9 years (IQR = 7.1-11.8 years) underwent Goldmann perimetry with KPRM and EBAR scoring. A KPRM could be undertaken in all children. A sample individual KPRM calculation (Figure 13, pg. 69) shows distances (degrees), starting in the supero-temporal field, and working clockwise of: 12.91, 1.82, 0.23 and 2.25, thus giving a KRPM score of 2.0 i.e. a median of these four values.

Table 14 shows the distribution of KPRM by EBAR (test quality) category. The median KPRM score increases with decreasing test quality (Kruskal-Wallis, p=0.005).

Table 14. KPRM score by Examiner Based Assessment of Reliability (EBAR) rating

Examiner Based Assessment of Reliability (EBAR) rating	Number of subjects	Median Kinetic Perimetry Reliability Measure (KPRM) score (IQR)
Good	91	1.5 (1.0 - 2.1)
Fair	10	3.4 (0.9 - 4.7)
Poor	2	18.3 [6.8 - 29.8]*

** Values indicate data range*

Figure 21 (below) illustrates KPRM points for subjects with varying test quality, showing an increase in KPRM score with reducing test quality.

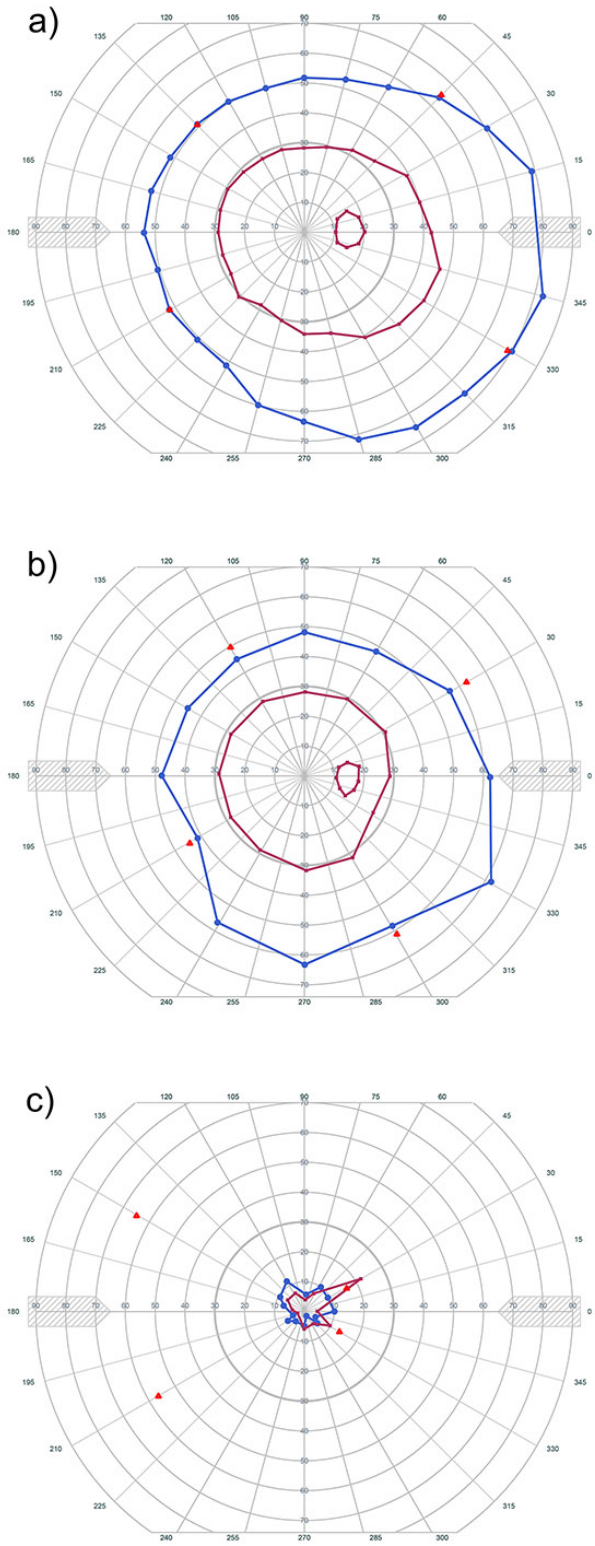


Figure 21. KPRM (triangles) plotted for good quality (top), fair quality (middle) and poor quality (bottom) VF tests.

5.1.4 Self-report of test difficulty

Participants reported testing with the Goldmann perimeter to be the easiest (63.3% rated as easy) and with the Humphrey to be the most difficult (24.2% rated as difficult). No relationship was found between subjective experience of test difficulty and examiner-rated test quality (Goldmann (p=0.305), Octopus (p=0.146) and Humphrey (p=0.166)).

Notably, 39/154 (25.3%) of all children, mostly those aged ≤8 years (33/39), commented on, or responded to, the audible noise of stimulus presentation for Octopus perimetry. Of these, in 17 children (11% of the total sample), this was reported by the examiner to have impacted on test quality. For Humphrey perimetry 33/154 (21.4%) of subjects reported factors such as the speed of stimulus presentation (including the relentless intensity of the task), the effect of testing to threshold (numerous stimuli that were difficult to see), and the varying locations of stimuli to be responsible for perceived difficulty.

5.1.5 Repeatability of perimetry in children

43/154 (27.9%) of children returned for a repeat assessment within 6 months of the original test with a mean follow-up time of 108 days (SD = 42). This subsample had a similar age distribution to the overall sample (children aged 5-6 years (n=16), 7-8 years (n=13), 9-11 years (n=7) and 12-15 years (n=7)).

Bland-Altman plots for Goldmann and Octopus isopter areas for children with 'good' quality (EBAR) tests at both visits showed good agreement for any isopter, indicating good test repeatability on both perimeters. No relationship between isopter area and age was found for any isopter on either perimeter.

Good agreement was found between the two visits for Humphrey perimetry mean deviation (MD) values (Bland-Altman, Mean difference = -0.24dB (95%CI: [-3.6, 0.7]).

5.1.6 Normative values

Only tests rated as 'good' quality (by examiner rating) for reliability were included in the analysis of normative data i.e. those tests performed to a level that would give results representative of true visual field sensitivity (Goldmann *n*=125, Octopus *n*=100, Humphrey *n*=98), rather than cases where co-operation affected results.

5.1.6.1 Kinetic perimetry

Visual field area and age were fitted to linear regression models for both perimeters and each isopter (Figure 22Figure 23, below).

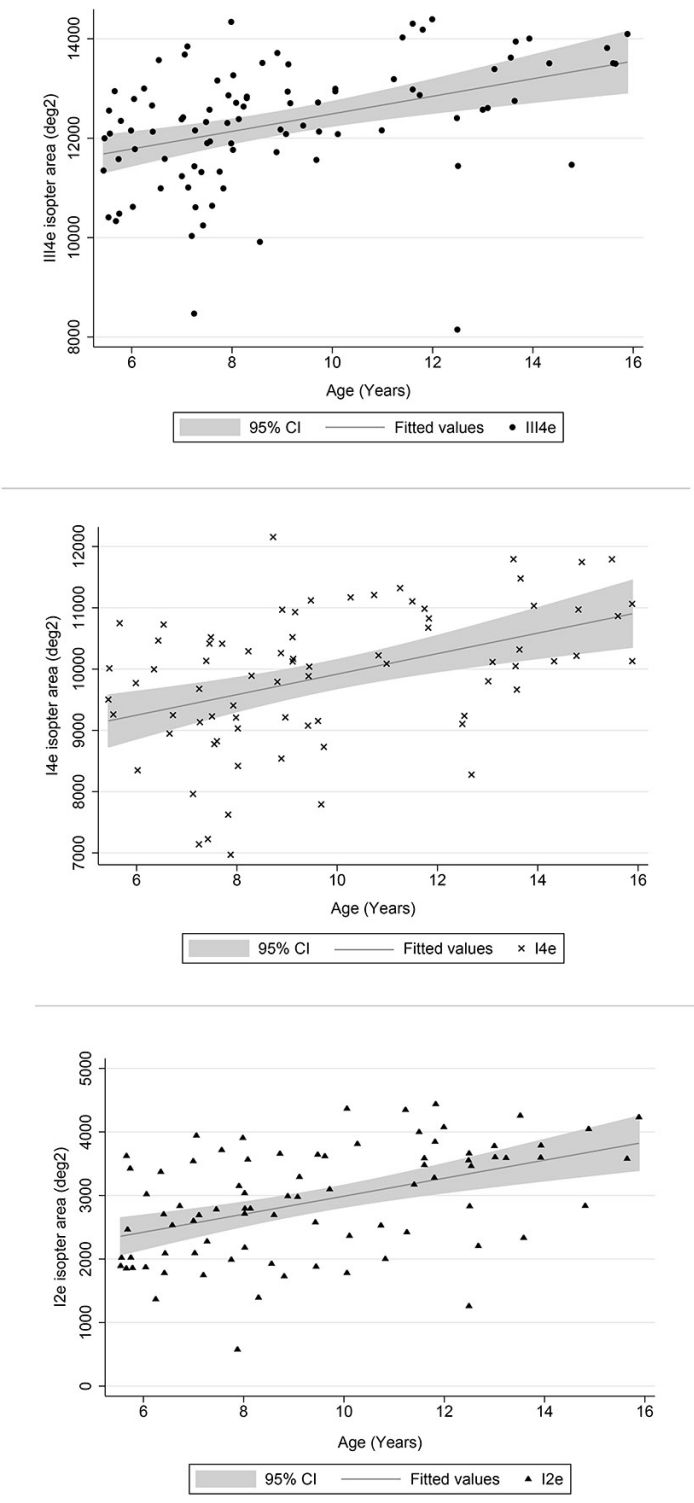


Figure 22. Goldmann visual field area vs. age for isopters III4e, I4e and I2e

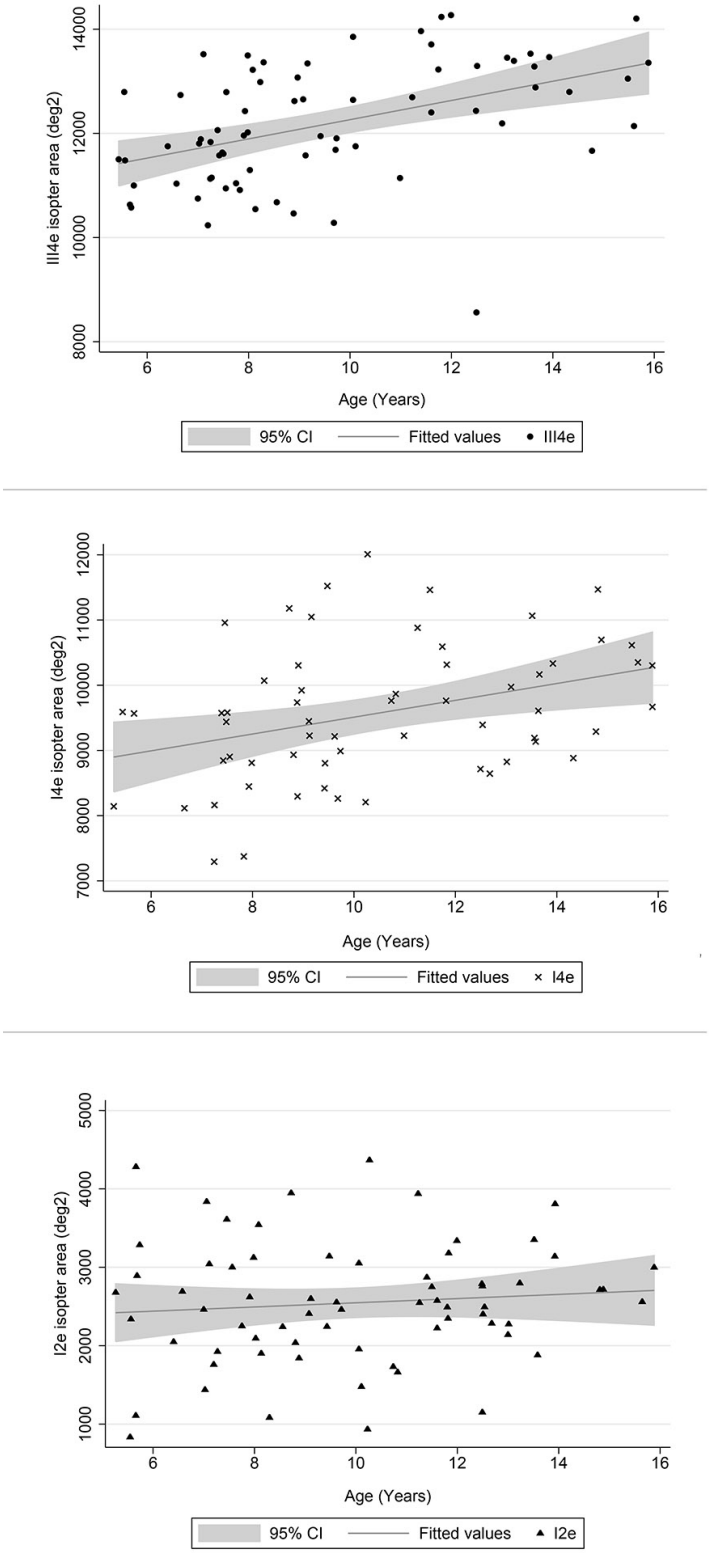


Figure 23. Octopus visual field area vs. age for isopters III4e, I4e and I2e

Model coefficients of 176.67 (III4e, 95% CI: [93.8, 259.5]), 167.32 (I4e, [86.4, 248.2]) and 141.7 (I2e, [80.9, 202.5]) were found for Goldmann isopters. These represent

the change in area (deg^2) for each additional year of age from 5 to 15 years. For Octopus isopters coefficients of 184.4 (III4e, [98.9, 269.8]), 129.1 (I4e, [39.6, 218.5]) and 26.7 (I2e, [-40.9, 94.4]) were found. With each perimeter there was a significant increase in visual field area with age with all isopters except Octopus I2e. Table 15 (below) lists mean isopter area, by age group for the three isopters tested using Octopus perimetry. These values are generated by the Octopus during isopter formation and provide clinically comparable data. Table 16 (below) lists mean isopter area for Goldmann perimetry, providing a comparison to Octopus values.

Table 15. Octopus perimetry normative isopter areas

Age group (years)	Mean (SD) isopter area (deg^2)		
	III4e	***I4e***	***I2e***
5-6	11426 (806)	8854 (837)	2463 (996)
7-8	11867 (977)	9213 (1084)	2518 (856)
9-11	12627 (1140)	9843 (1149)	2560 (764)
12-15	12731 (1283)	9807 (832)	2605 (596)

** Values shown here are not for reaction-time corrected isopters and were formed from straight, not curved (spline), points.*

Table 16. Goldmann perimetry normative isopter areas

Age group (years)	Mean (SD) isopter area (deg^2)		
	III4e	***I4e***	***I2e***
5-6	11862 (915)	9730 (758)	2468 (683)
7-8	12026 (1268)	9278 (1252)	2625 (852)
9-11	12947 (826)	10257 (950)	3244 (808)
12-15	12798 (1494)	10410 (974)	3332 (794)

Normative kinetic data were analysed and displayed graphically to allow clinical interpretation. A variety of methods was available for use, and these are detailed

below. These examples use children aged 8-11 years, tested with Goldmann perimetry (isopter I4e), including only those with 'good quality' assessments (*n*=30).

Raw data are shown as points (Figure 24) and lines (Figure 25) below, to enable visualisation of the statistical summary process. From this, it is evident that each meridian has its own independent distribution that is non-normally distributed.

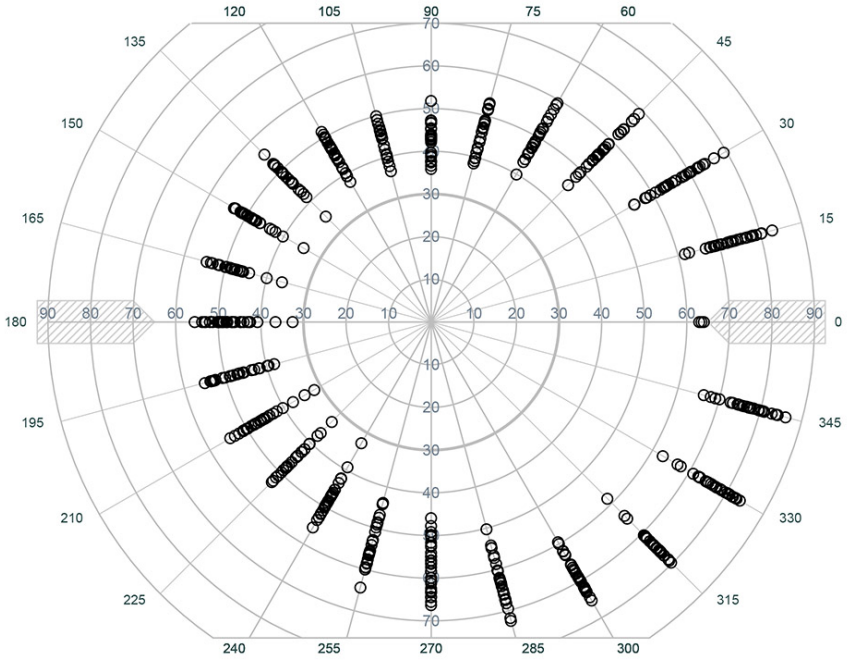


Figure 24. Raw data points for Goldmann isopter I4e

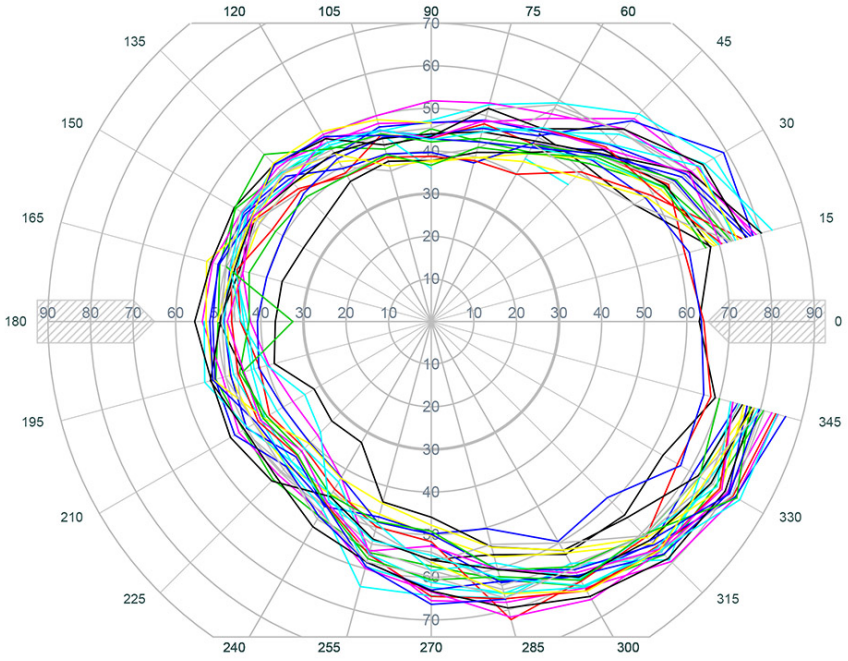


Figure 25. Raw data lines for Goldmann isopter I4e

Firstly, isopters were summarised using a mean and 95% CI, a parametric method, with variance calculated at each meridian (Figure 26 and Figure 27, below). This method does not account for the relationship *within* subject – i.e. accounting for

each subject contributing multiple data points to an isopter (demonstrated in Figure 25, above).

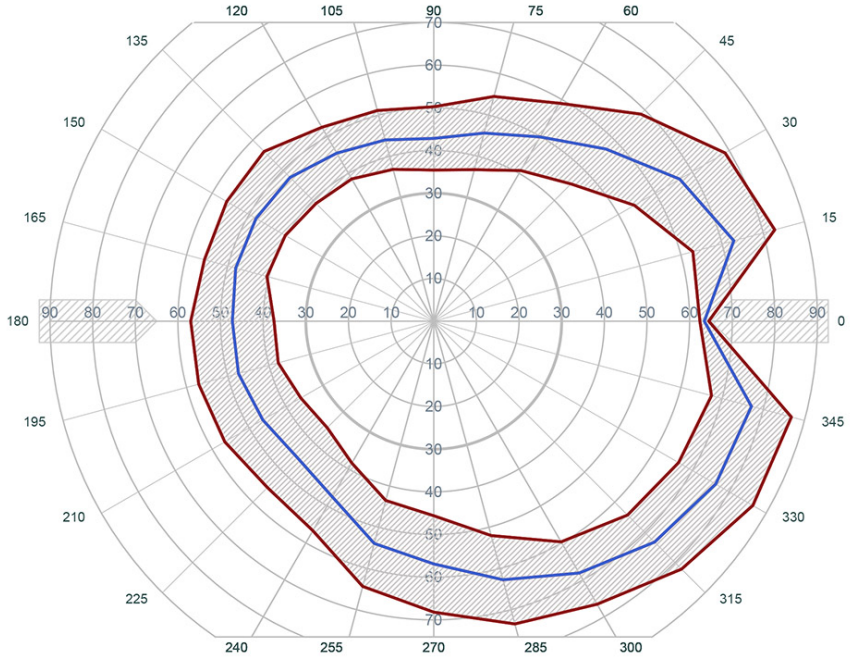


Figure 26. Normative isopter distribution summarised with a mean line and 95% CI, using all data points

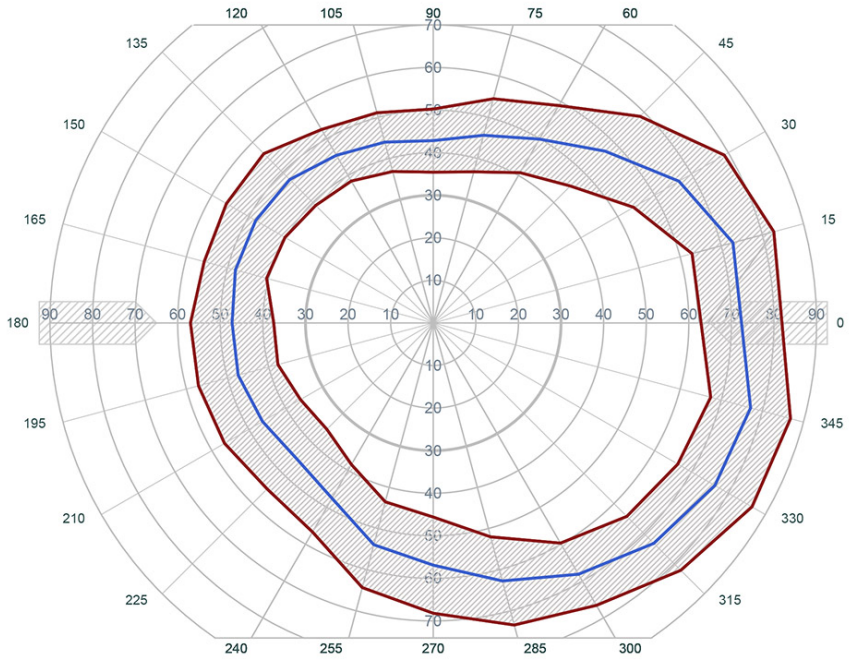


Figure 27. Normative isopter distribution summarised with a mean line and 95% CI, omitting data points at 90 degrees

Figure 28 (below) explores distribution using quantiles. A change in distribution is noted, reflecting that data along each meridian are non-normally distributed. This method provides a better fit to the data, but still fails to effectively summarise the effect of variation within an individual.

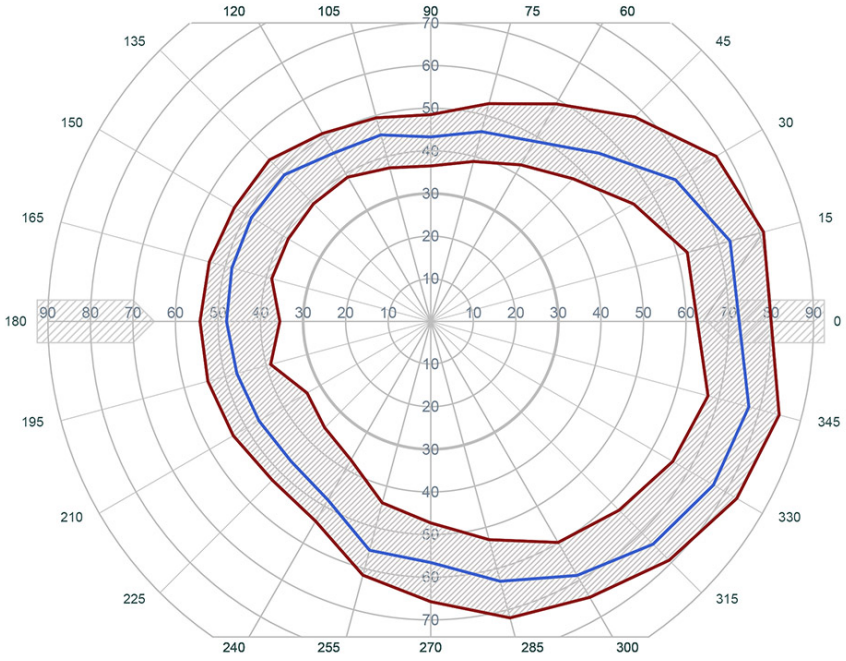


Figure 28. Normative isopter distribution summarised with a mean line and quantiles encompassing 95% of data, omitting data points at 90 degrees

Isopter data may show conditional distributions that do not conform to normality assumptions, such as symmetry and constant variance (homoscedasticity), either on the observed or the transformed (e.g. logarithmic) scale of the outcome. For these reasons, modelling based on mean (normal) regression can lead to incorrect inference. Even when approximate normality is achieved after transformation, back-transformation of conditional expectations is troublesome as it may lead to estimates and/or confidence regions outside the admissible range of the outcome (i.e. bowl surface). Moreover, as discussed earlier, isopter data that are collected repeatedly on the same subject are correlated by design. While mixed-effects

models for the mean account for the clustered design, they are still subject to strong distributional assumptions and back-transformation issues. Thus, further exploration for a suitable statistical model led to fitting linear quantile mixed-effects regression models based on the asymmetric Laplace distribution. These models introduce weak assumptions on the distribution of the error and therefore are robust to deviations from normality. They also allow for inclusion of subject-specific effects i.e. within-subject correlation resulting from repeated measurements.

The linear predictor of the model was chosen by minimising Bayesian Information Criterion (BIC) and included a random intercept (b_0) and a fixed effect for the interaction between cosine and sine terms (β_5), along with fixed effects for individual cosine and sine terms. This model can be written as:

$$r = (\beta_0 + b_0) + \beta_1 \cos(\theta) + \beta_2 \sin(\theta) + \beta_3 \cos(2\,\theta) + \beta_4 \sin(2\,\theta) + \beta_5 \sin(\theta) \times \cos(2\,\theta) + \varepsilon_p\,,$$

where ε_p is a random error term whose $100 \cdot p$th centile is constrained to be zero.

Figure 29 shows how the final model fits the sample data from Figure 25. These raw data are super-imposed (in Figure 30) emphasising, particularly in the nasal field, the effect of accounting for non-normal distribution, and within subject variation. The final model shown here allows for fitting of data, respecting the clinical context of a kinetic visual field test i.e. accounting for each individual contributing multiple (and thus linked) data points.

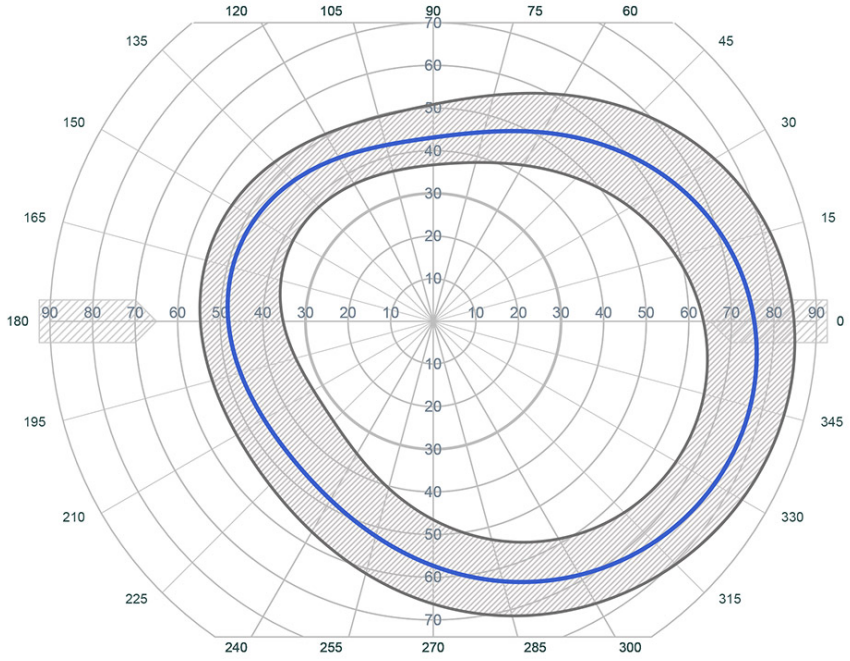


Figure 29. Normative isopter distribution summarised by a linear quantile mixed-effects regression model

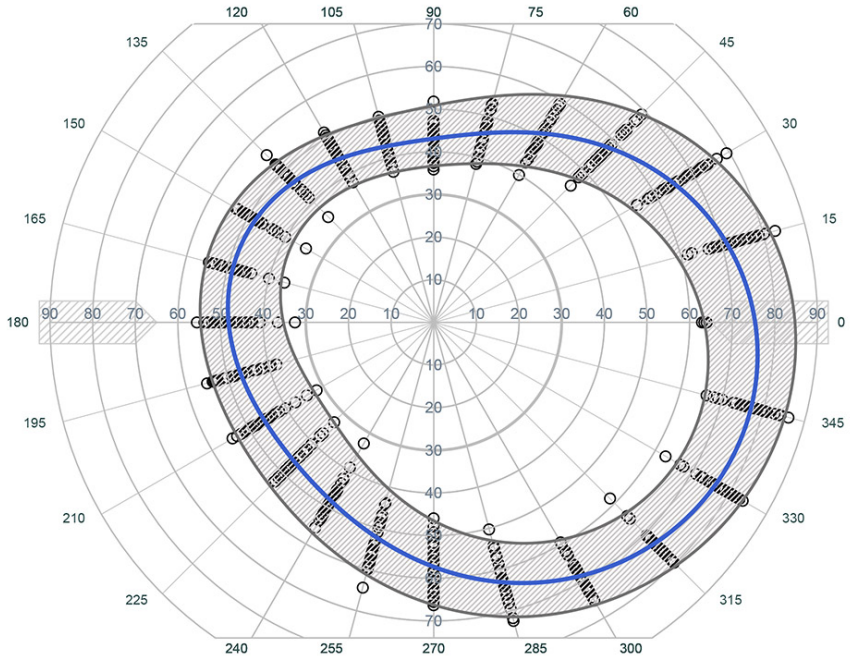


Figure 30. Normative isopter distribution summarised by a linear quantile mixed-effects regression model, with super-imposed raw data points

The linear quantile mixed-effects regression model (lqmm) was then used to generate normative values for Goldman and Octopus kinetic perimetry. Figure 31A to D show these data for isopters III4e (black), I4e (blue) and I2e (red).

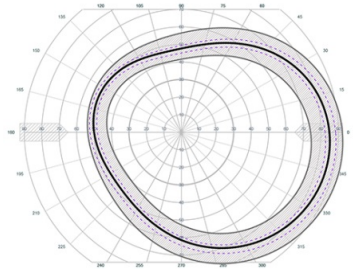
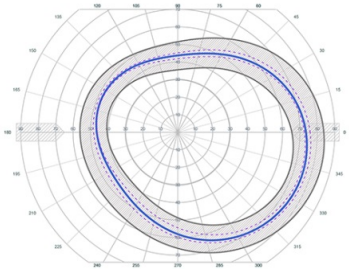
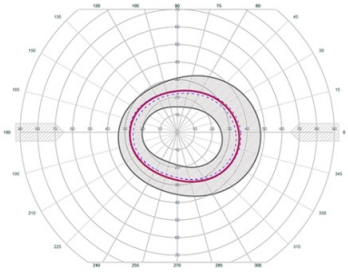
III4e	I4e	I2e
		

Figure 31A. Goldmann isopters, subjects aged 5-6 years

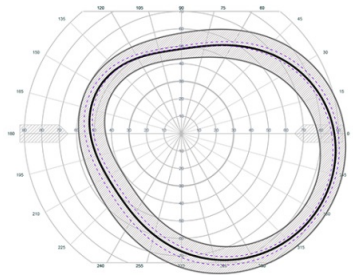
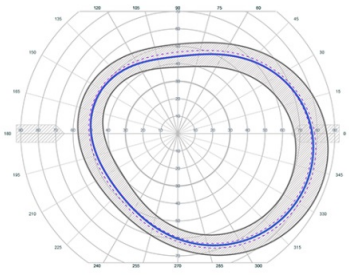
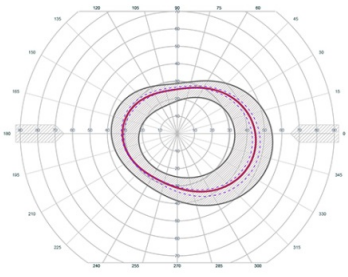




Figure 31B. Goldmann isopters, subjects aged 13-15 years

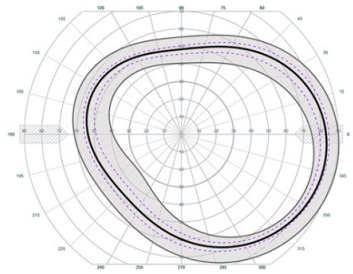
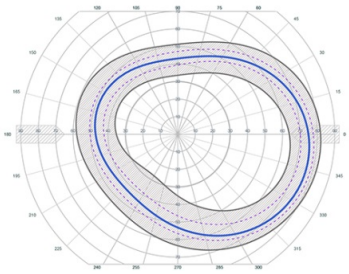
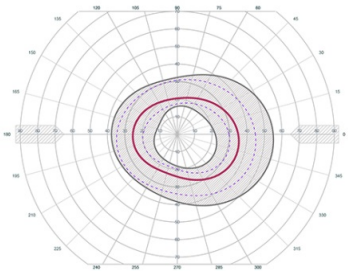




Figure 31C. Octopus isopters, subjects aged 7-8 years

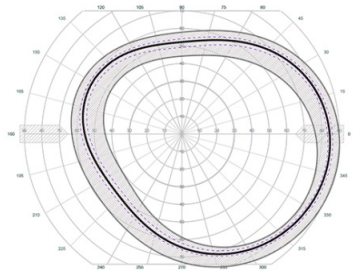
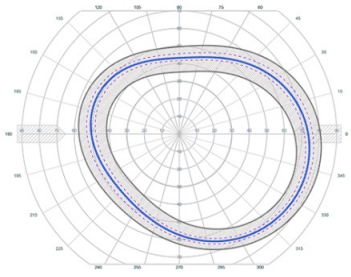
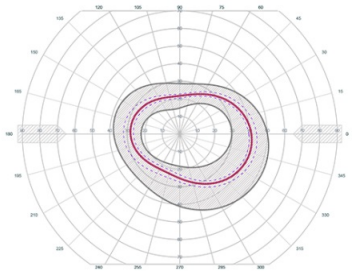




Figure 31D. Octopus isopters, subjects aged 13-15 years

Figure 31. Normative data for kinetic perimetry by age group

**The central, thick band shows median values, with the dashed (purple) lines encompassing the central 50% of data (interquartile range). The grey, hashed region delineates the area*

containing 95% of the data. As fewer young children were able to complete Octopus perimetry to a 'good quality' rating, the 'lqmm' regression model was not sufficiently robust to use in the youngest group. Thus, children aged 7-8 years are shown in Figure 31C.

Figure 31 (above) demonstrates differences in VF area by age for Octopus and Goldmann perimetry, with greatest change in the temporal and infero-temporal field. Isopter III4e demonstrates a 'ceiling effect' when reaching the limit of the Goldmann perimeters' testing area. The inner 2.5% quantile line shifts towards a more eccentric position with age for all isopters on both perimeters, and there is a slight narrowing of the 95% region in older subjects, indicating reduced variability in responses with increasing age.

Normative templates were generated for both kinetic techniques and have been made available for download on a non-commercial licence (http://e-lucid.com/i/video_and_images/optic_templates.html).

5.1.6.1.1 Comparability of Goldmann and Octopus perimetry

Bland-Altman plots of kinetic isopter area, for Goldmann and Octopus perimetry, are shown in Figure 32-Figure 34 (below), showing mean difference (centre line) and upper/lower limits of agreement. The area values showed good agreement for all isopters (III4e: p=0.224, I4e: p=0.205, I2e: p=0.376). There was a mean difference of 187.4 deg^2 (95% CI: -23.7, 398.6) for isopter III4e, 412.1 deg^2 (242.7, 581.4) for isopter I4e, and 487.3 deg^2 (344.2, 630.4) for isopter I2e.

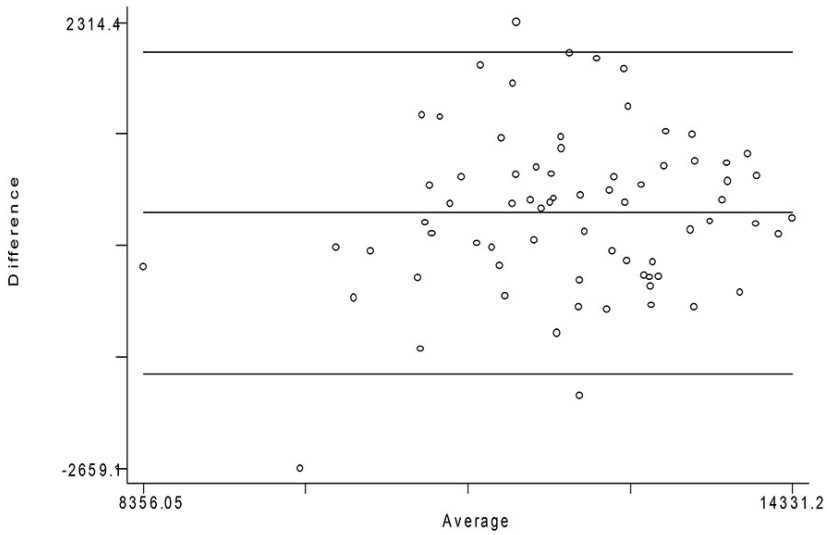


Figure 32. Bland-Altman plot of isopter III4e area, comparing Goldmann and Octopus perimeters

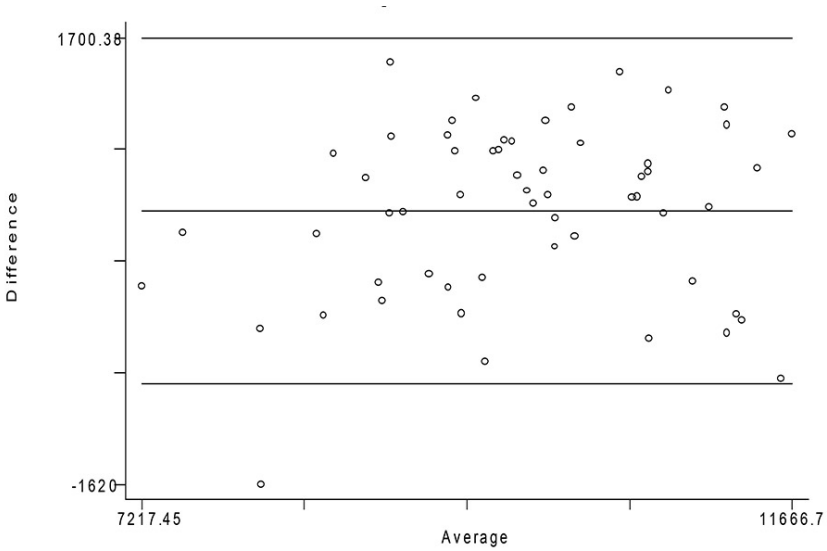


Figure 33. Bland-Altman plot of isopter I4e area, comparing Goldmann and Octopus perimeters

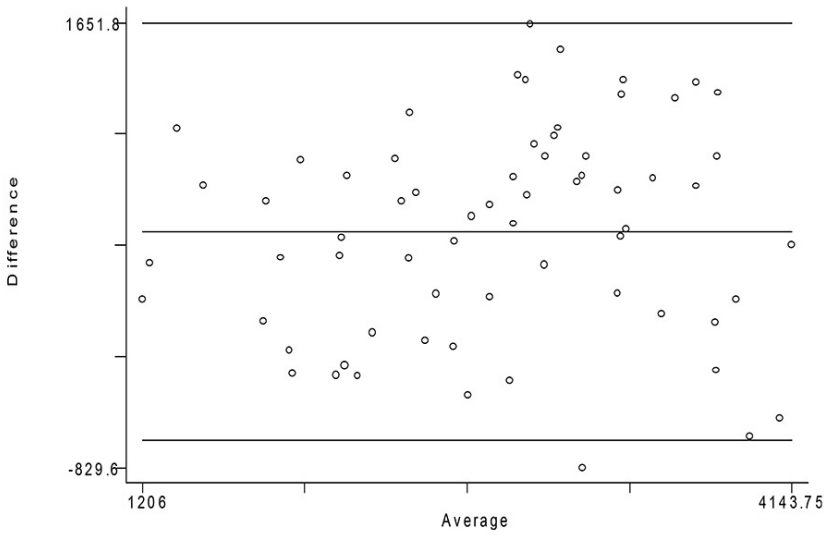


Figure 34. Bland-Altman plot of isopter I2e area, comparing Goldmann and Octopus perimeters

Lqmm plots of kinetic field data (Figure 35-Figure 36, below) show that whilst there is good agreement in isopter area between the two kinetic perimeters, isopter shape and normative confidence bands differ.

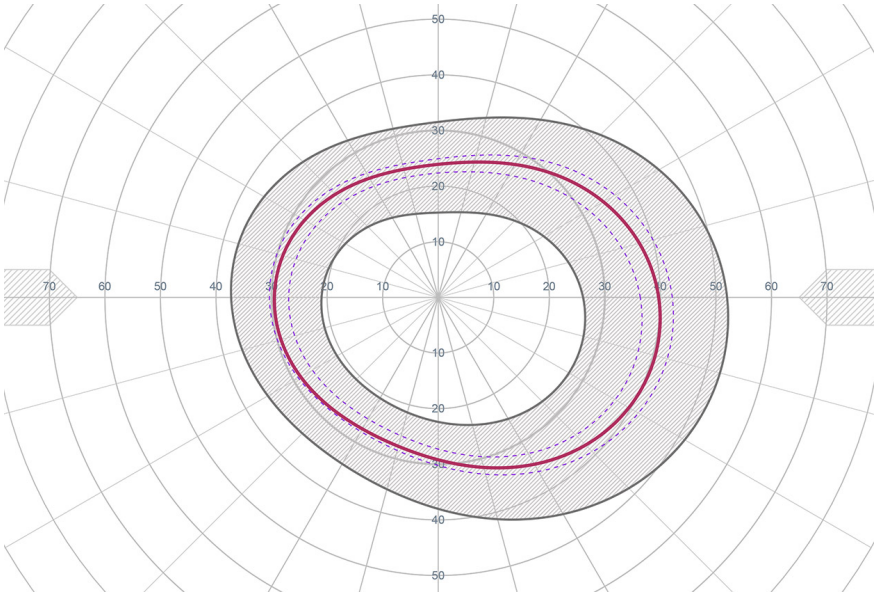


Figure 35. Lqmm model for Goldmann isopter I2e in children aged 8-11 years

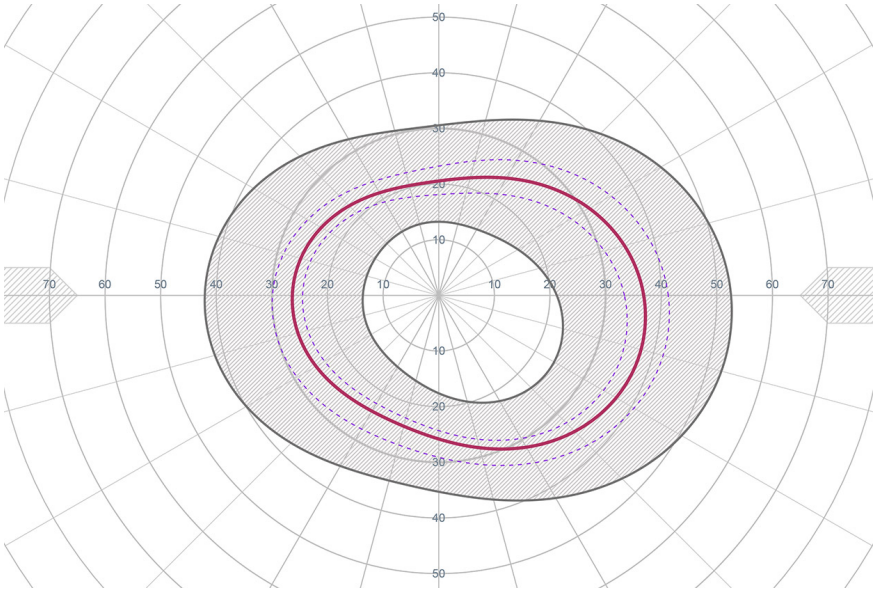


Figure 36. Lqmm model for Octopus isopter I2e in children aged 8-11 years

Mean blind spot area for Goldmann perimetry was 80.6 deg^2 (SD=27.7) and 63.5 deg^2 (SD=29.2) for Octopus perimetry. No relationship between blind spot size and age was found for either perimeter (Goldmann (p=0.745), Octopus (p=0.074).

5.1.6.2 Static perimetry

Analysis of Mean Deviation (MD) (a summary statistic produced by the Humphrey perimeter) gives information regarding central visual field sensitivity. Regression analysis revealed an association between age and MD, and further analysis by piecewise regression (Figure 37) suggests a point of change in this relationship at 12 years of age.

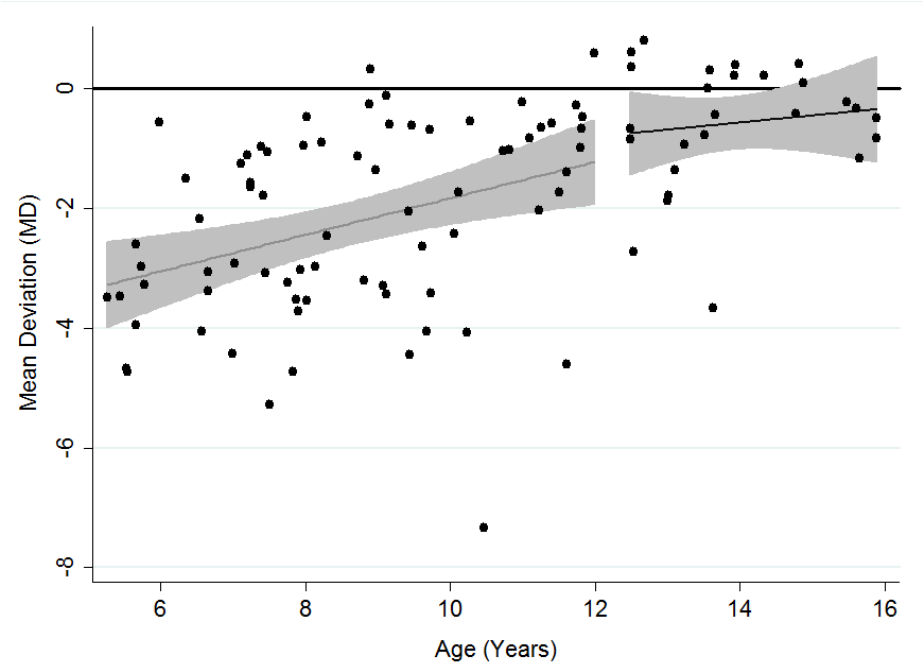


Figure 37. Piecewise regression of Humphrey Mean Deviation (MD) scores with age

Between ages 5-12 years, there is a co-efficient of 0.30 (i.e. a 0.3dB increase in sensitivity per unit increase in age, 95% CI: [0.21, 0.40]). After 12 years of age, there is no significant association (p=0.526) and MD values are similar to adult levels i.e. average MD ≈ 0 (see Table 17, below).

Table 17. Average Mean Deviation (MD) values by age group (Humphrey SITA 24-2 FAST)

Age (years)	Average MD value (SD)
5-6	-3.22 (1.16)
7-8	-2.15 (1.42)
9-11	-1.85 (1.75)
12-15	-0.58 (1.05)

5.2 Glaucoma group (Group B)

5.2.1 Sample characteristics

Between June 2013 and May 2015, 82 children were approached to take part in this phase of the study. 68/82 (82.9%) agreed to participate. 3 children subsequently failed to attend for their appointment. Thus, 65 children consented and participated in the study – giving a participation rate of 79.3%. Participant age and sex demographics are shown in Figure 38 (below). The median age of subjects was 12.2 years (IQR: 9.3-14.2) with 33 (50.8%) females. Participants were predominantly White (*n*=51 (78.5%)), with 9.2% Black, 7.7% Asian and 4.6% Mixed ethnicity.

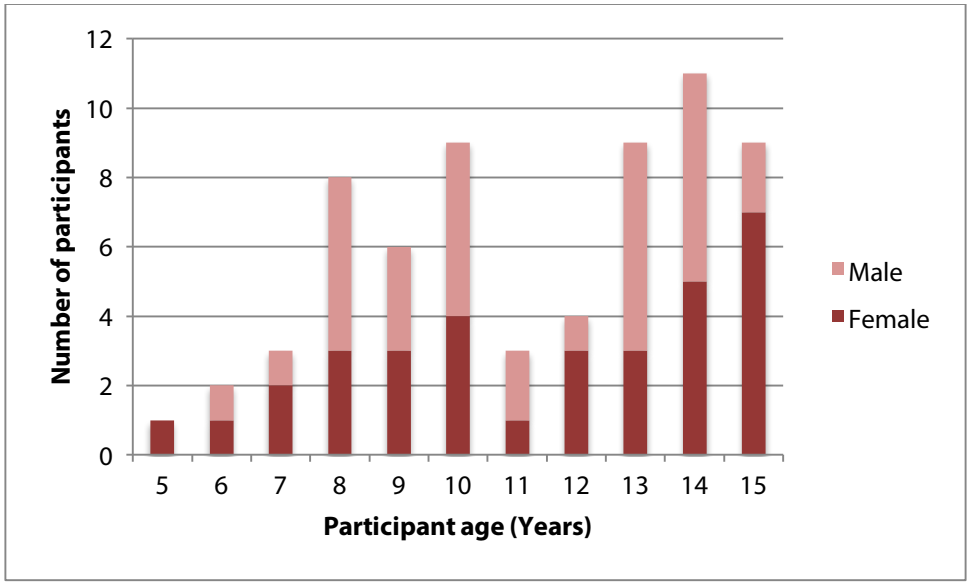


Figure 38. Group B (glaucoma) sample dempgraphics by age and sex (*n*=65)

Eighteen (27.7%) subjects had no previous perimetric testing experience. Of these, 13 (72.2%) were less than 10 years of age. 47 subjects had prior experience ranging from 1 to 8 years (median of 2 years' experience (IQR: 1-4years)), with a median of 1 test (IQR: 1-1.5) per year.

Table 18 (below) lists ophthalmic diagnoses for all subjects in this sample, using the most recent international classification system of childhood glaucoma.[103]

Table 18. Classification of glaucoma diagnosis for participants (*n*=65)

Ophthalmic diagnosis	**Number of subjects (*n*)**	
	Unilateral	Bilateral
Primary congenital glaucoma	7	22
Juvenile open-angle glaucoma	0	6
Primary angle-closure glaucoma	0	1
Primary glaucomas associated with systemic diseases		
- Sturge-Weber syndrome	2	0
- Neurofibromatosis (NF-1)	1	0
Primary glaucomas with profound ocular anomalies		
- Aniridia	0	1
- Axenfeld-Rieger anomaly	0	2
- Posterior polymorphous dystrophy	1	0
Secondary glaucomas		
- Traumatic glaucoma	1	0
- Glaucoma related to a port wine stain	2	1
- Glaucoma related to chronic uveitis	1	6
- Glaucoma following lensectomy for congenital cataracts	1	8
Glaucoma suspect	0	2
Total	**65**	

One subject withdrew after the first perimetric test, citing time constraints as a reason for being unable to continue with the study. Humphrey data for this subject are presented where appropriate.

Seventeen subjects had only one 'affected' eye. Thus, the sample potentially included 113 eyes with glaucoma, as shown in Figure 39 (below). Three right eyes and 2 left eyes were not assessed due to severely reduced VA (worse than 1.3 LogMAR). These subjects all had bilateral glaucoma. Thus in total, 125 eyes were tested, of which 108 had glaucoma.

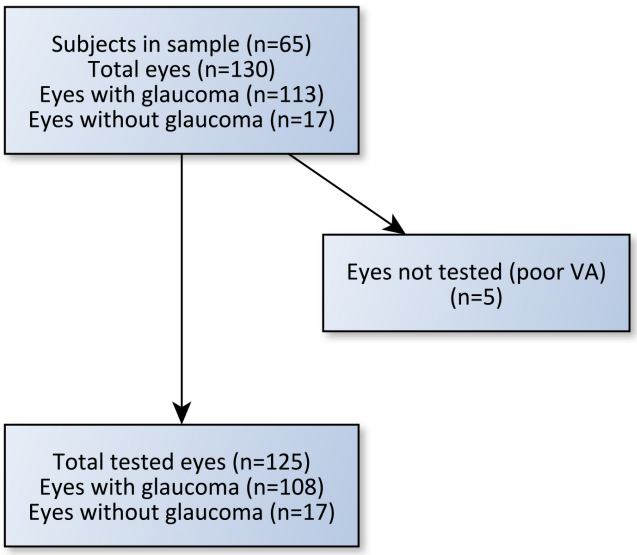


Figure 39. Flowchart describing affected/unaffected eyes for participants in Group B (glaucoma)

Median LogMAR acuity of the 108 tested eyes with glaucoma was 0.22 (IQR: 0.04 to 0.4), and 0.0 (0 to 0.03) for fellow eyes. Median spherical equivalent of tested glaucomatous eyes (*n*=108) was 0.0D (IQR: -2.0 to 1.0) (Figure 40). Fellow eyes had a median spherical equivalent of 0.0D (IQR: 0.0 to 0.25).

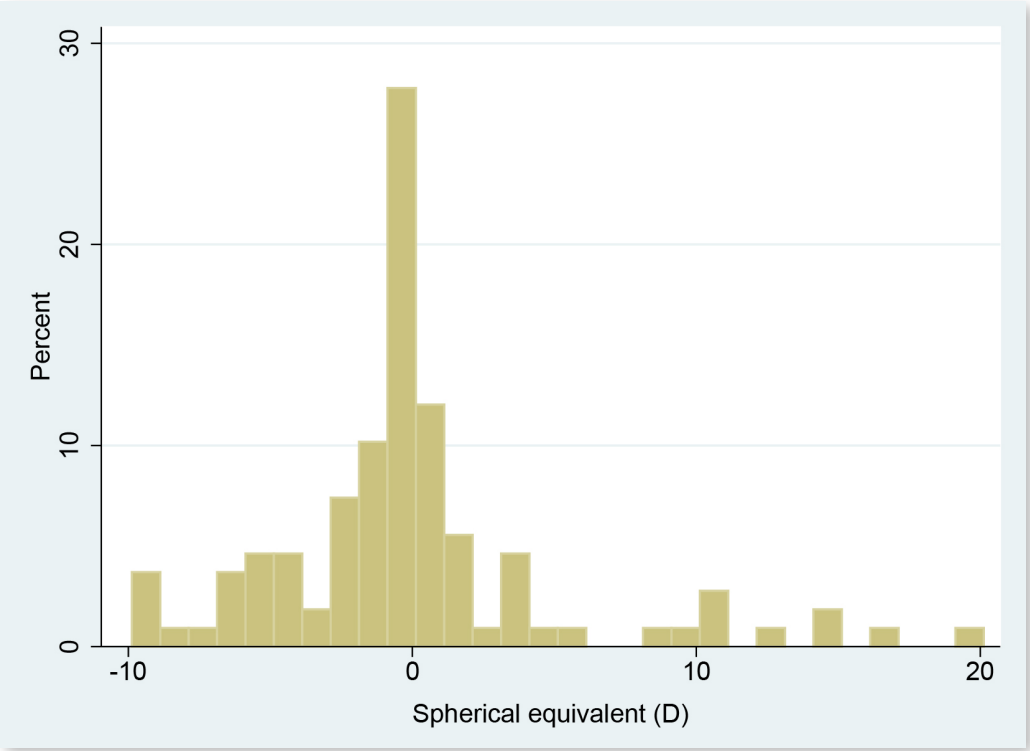


Figure 40. Spherical equivalent (D) in tested glaucomatous eyes (*n*=108)

5.2.2 Feasibility of perimetry

5.2.2.1 Test completion

All subjects (*n*=65) completed the Humphrey assessment. 63/64 (98.4%) completed the combined static/kinetic Octopus assessment (Table 19, below). The child who failed to complete an Octopus assessment, reporting being unable to see the central fixation target with one eye (VA = 1.0 LogMAR), was nevertheless able to complete a Humphrey assessment with both eyes.

5.2.2.2 Test duration

Table 19 (below) summarises test duration for both perimeters, by age group.

Table 19. Participant demographics and test feasibility for both perimeters (*n*=65)

Age group (years)	Sex		Number completing assessments (%)		Mean test duration (min) (SD)	
	Male	*Female*	*Humphrey static*	*Octopus combined*	*Humphrey static*	*Octopus combined*
5-7	2	4	6 (100)	6 (100)	18 (3.1)	20.2 (4.8)
8-11	15	11	26 (100)	24 (96)	13.1 (3.3)	16.3 (3.7)
12-15	15	18	33 (100)	33 (100)	12.8 (2.8)	16.5 (2.9)

** Test duration values include preparation and assessment tasks*

Duration of assessment with a combined static/kinetic test using the Octopus (see methods pg. 76) was significantly greater than static perimetry on the HFA ($p<0.001$).

Humphrey test duration declined with decreasing severity of visual field loss ($p<0.001$) and increasing EBAR ratings ($p=0.006$) in a linear regression model clustered by subject (n subjects = 60) modelling associations with MD, VA, IOP, age and test quality. Octopus perimetry test duration was unaffected by MD, VA, IOP and test quality, but reduced with increasing age ($p=0.02$).

9/65 (13.9%) children required a rest break during Humphrey assessment, but only 3/64 (4.7%) during Octopus perimetry. Most (11/12) children needing a break were aged 8 years or under.

5.2.3 Quality/Reliability of perimetry

The quality of each perimetric assessment was rated using the EBAR scoring system (categories of 'good', 'fair' or 'poor' quality), as shown in Figure 41 (below).

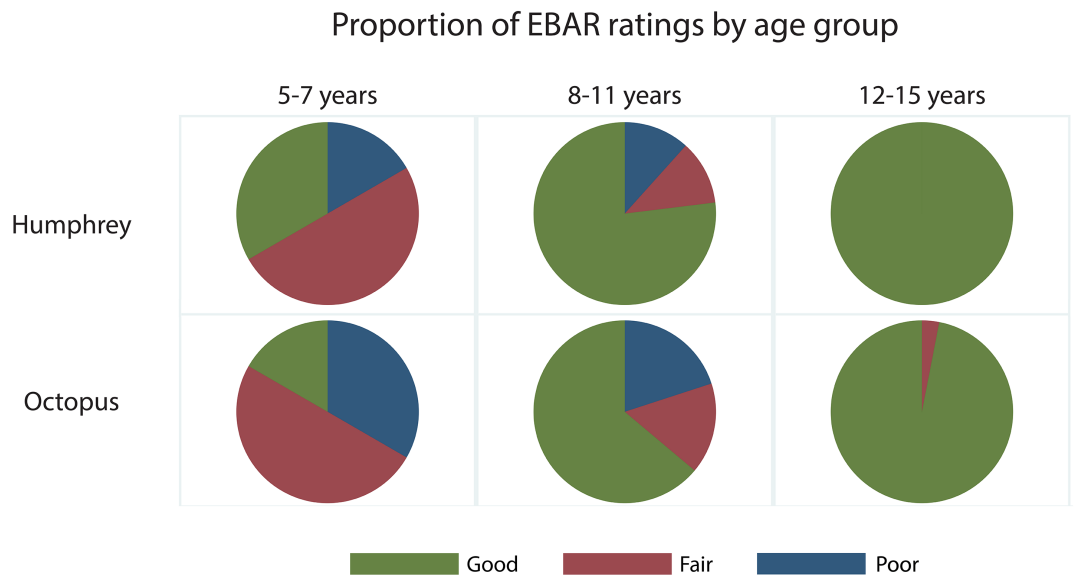


Figure 41. Proportion of EBAR (test quality) ratings per perimeter, by age groups for children with glaucoma

Quality/reliability (measured with EBAR) improved with increasing age for both Humphrey (p=0.002) and Octopus perimeters (p<0.001). In children over 10 years of age, no significant difference was found between the EBAR ratings of Humphrey and Octopus assessments (χ^2, p=0.827). In children under 10 years of age, EBAR scores were better for Humphrey perimetry (χ^2, p=0.005).

EBAR scores for young children (aged 5-7 years) were worse in those with glaucoma, compared to those without VF loss (group A (Figure 20, pg. 97)). However, children over 10 years of age with glaucoma routinely show good reliability assessments with only 3/90 (3.3%) assessments (n=45) not rated as 'good quality'.

As noted earlier, younger children were also the least experienced. Table 20 (below, pg. 126) shows that of the 10 Humphrey and 15 Octopus assessments with a 'fair'/'poor' quality rating, 90% and 66.6% respectively, had no prior experience of testing.

Table 20. Comparison of perimetric test experience and EBAR (test quality) rating

Perimeter	Perimetric experience?	EBAR rating			
		Good	Fair	Poor	Total
Humphrey	Yes	46	0	1	47
	No	9	6	3	18
Octopus	Yes	42	2	3	47
	No	7	6	4	17

For Humphrey perimetry, there was a significant reduction with increasing age in the number of false positives (p=0.011) and fixation losses (p=0.003). No change with age was noted for false negative values (p=0.107). Similarly, for Octopus perimetry, there was a significant reduction with age in the number of false positives (p<0.001), and no change with age for false negative values (p=0.251).

Table 21 (below), shows a comparison of EBAR ratings with automated reliability indices (false positives and fixation losses).

Table 21. Comparison of EBAR (test quality) with automated reliability indices for Humphrey perimetry, in children with glaucoma.

EBAR Rating	False Positives		Fixation Losses		Traditional Reliability Indices*	
	<15%	*≥15%*	*<25%*	*≥25%*	*Reliable*	*Unreliable*
Good	99	8	56	51	53	54
Fair	7	3	2	8	2	8
Poor	3	5	1	7	1	7
Total	109	16 (13%)	59	66 (53%)	56	69 (55%)
	125		125		125	

** Traditional reliability indices are defined here as fixation losses ≥ 25% or false positives ≥15%*

Traditional RI's disagreed with EBAR in 55/125 cases (44%). Taking false positives alone showed better agreement with EBAR ratings (104/125 (83%)).

5.2.4 Perimetry in unaffected eyes

In those with unilateral glaucoma (*n*=17), median MD in unaffected eyes was -0.41dB (IQR = -1.64 to 0.28) with Humphrey perimetry and -0.4dB (IQR = -1.4 to 0.1) with Octopus perimetry (*n*=17). These values lie within expected normative ranges as shown in Table 17 (pg. 119).

Two subjects demonstrated kinetic isopter values outside expected values. In each case, the examiner noted problems with test co-operation.

5.2.5 Detection of VF defects

5.2.5.1 Humphrey vs. Octopus static

Analysis of eyes affected by glaucoma (*n*=82, good EBAR only) showed good correlation (*r*=0.93) between Humphrey MD and Octopus MD values. Figure 42 (below) demonstrates the relationship between Humphrey MD and Octopus MD

for those with good EBAR ratings for both tests (*n*=93, correlation co-efficient = 0.94). However, there is evidence that this relationship is weaker for Octopus MD values below -6 dB i.e. moderate/dense VF defects.

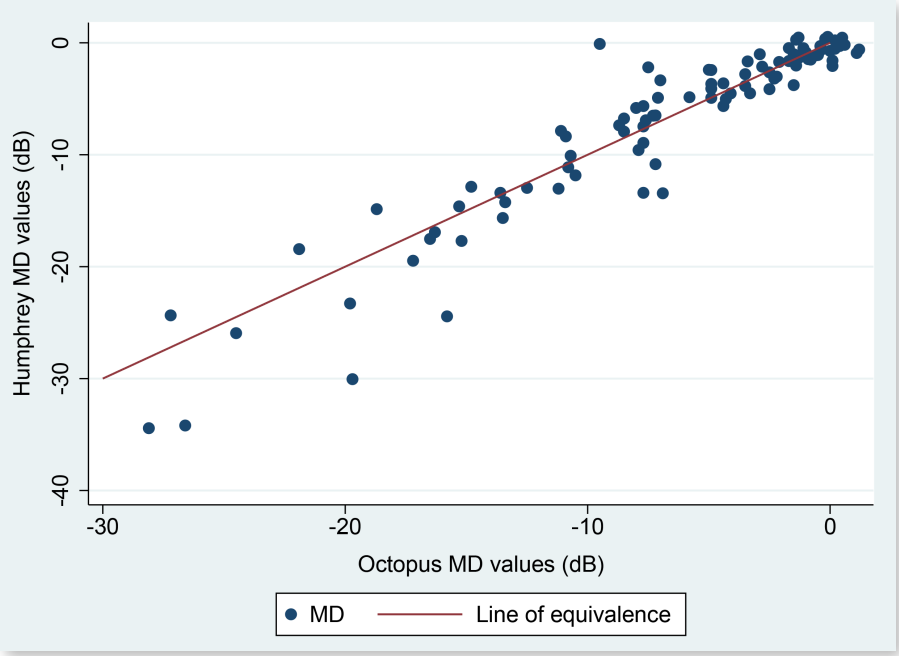


Figure 42. Octopus vs. Humphrey MD values

Bland-Altman analysis of Humphrey and Octopus MD (good EBAR) for values octopus MD >-6dB (Figure 43, *n*=50) shows good agreement between values (*p*=0.238). Values below -6dB (*n*=43) do not show good agreement (Bland-Altman, *p*<0.001), which could be explained by greater inherent variability in testing those with severe VF defects.

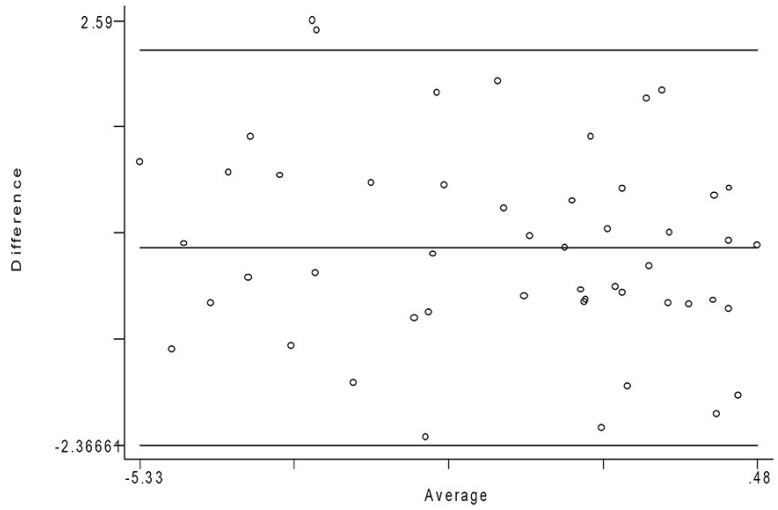


Figure 43. Bland-Altman plot of Humphrey and Octopus MD values for Octopus MD>-6

Humphrey PSD and Octopus sLV values are not comparable and significantly differ (p<0.001).

Table 22 (below) shows Humphrey and Octopus classification scores of disease status (Table 10, pg. 88) for glaucomatous eyes. Analysis using a linear weighted kappa technique showed 'substantial' agreement between values (κ=0.79, good EBAR results only). 3/93 (3.2%) results reported a higher classification score for Humphrey perimetry, with 29/93 (31.2%) higher for Octopus. Taking Humphrey perimetry as the gold-standard – assessment with the Octopus occasionally underestimates loss in severe defects, but potentially detects defects earlier than Humphrey perimetry.

Table 22. Comparison of Humphrey and Octopus static classification scores in glaucomatous eyes

Humphrey classification score	Octopus static classification score						Total
	0	1	2	3	4	5	
0	11	7	0	0	0	0	**18**
1	0	8	5	2	0	0	**15**
2	0	1	4	5	0	0	**10**
3	0	0	0	16	6	0	**22**
4	0	0	0	2	6	0	**8**
5	0	0	0	0	0	7	**7**
Total	**11**	**16**	**9**	**25**	**12**	**7**	**80**

** Shaded areas represent equivalent scores.*

Table 23 (below) shows the comparison of classification scores for fellow (unaffected) eyes (good EBAR only), showing 4/11 (36.4%) of results rated as '0' for Humphrey perimetry as having a score ≥1 for Octopus perimetry. In total, 2/13 (15.4%, Humphrey) and 6/13 (46.2%, Octopus) results had a score >0.

Table 23. Comparison of Humphrey and Octopus static classification scores for unaffected eyes

Humphrey classification score	Octopus static classification score				Total
	0	1	2	3	
0	7	2	1	1	**11**
1	0	2	0	0	**2**
Total	**7**	**4**	**1**	**1**	**13**

** Shaded areas represent equivalent scores.*

5.2.5.2 Comparison between static and kinetic perimetry in children with glaucoma

Modelling Octopus kinetic isopter area against Humphrey MD shows that isopter I4e increases in size/area with an increase in MD (linear regression, coefficient = 435.7deg^2, 95% CI: 350.9-520.6) i.e. an increase of 435.7deg^2 per unit increase in MD (1dB). For isopter III4e (used in those with poor VA) the regression co-efficient was 204.4 deg^2 (95% CI: 83.1-325.7). Table 24 (below) shows the comparison of disease staging classifications for Humphrey static vs. Octopus kinetic perimetry for glaucomatous eyes, showing 'substantial' agreement (κ=0.61 (linear weighted), good EBAR results only). Fellow eyes are shown in (Table 25, pg. 132).

Table 24. Comparison of Humphrey and Octopus kinetic classification scores for glaucomatous eyes

Humphrey classification score	Octopus kinetic classification score						Total
	0	I	II	III	IV	V	
0	14	3	1	0	0	0	**18**
I	3	9	3	0	0	0	**15**
II	0	1	7	2	0	0	**10**
III	2	5	5	6	4	0	**22**
IV	0	1	0	3	4	0	**8**
V	0	0	1	2	2	2	**7**
Total	**19**	**19**	**17**	**13**	**10**	**2**	**80**

** Shaded areas represent equivalent scores. Scores of 2/3 were classified as equal for analysis of kinetic data.*

Table 24 (above) shows that 7 results were rated as grade V for Humphrey perimetry, with only 2 for kinetic perimetry, demonstrating the ability of kinetic perimetry to detect residual sensitivity outside 30° eccentricity.

Table 25. Comparison of Humphrey and Octopus kinetic classification scores for fellow eyes

Humphrey classification score	Octopus static classification score		Total
	0	1	
0	9	2	**11**
1	1	1	**2**
Total	**10**	**3**	**13**

** Shaded areas represent equivalent scores.*

5.2.5.3 Relationship between perimetric test outputs and other clinical features

Only VA was significantly associated with MD (p<0.001) (regression, modelling Humphrey or Octopus MD with associations of VA, IOP and age (good EBAR only, Humphrey n=101, Octopus n=88, clustered by subject)). When examining pattern standard deviation (PSD)/square root of loss variance (sLV) (see Glossary, pg. 185) rather than MD, no statistically significant associations were found. There was a strong relationship between VA and MD, yet there are a proportion of subjects that demonstrate both good VA with severe VF defects (Figure 44, below).

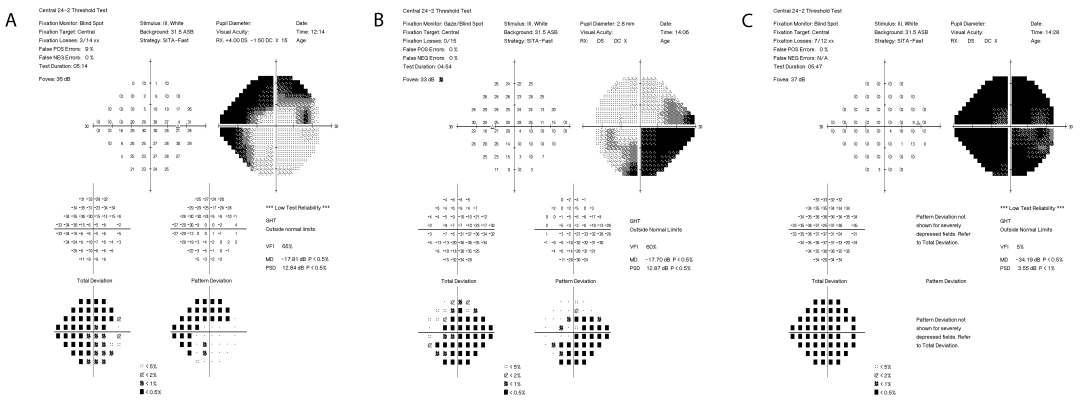


Figure 44. Glaucomatous VF defects with preserved central VA (between 0.0 and 0.1 LogMAR)

Figure 44 shows that preserved central VA can co-exist with solely peripheral defects outside ≈6° (Figure 44A) and in those whose defects extend close to the centre of the field (Figure 44B & C), leaving only the fovea unaffected. It is also possible to exhibit poor VA with preserved visual field sensitivity (Figure 45, below), thus reinforcing the importance of testing VA and undertaking perimetry in tandem.

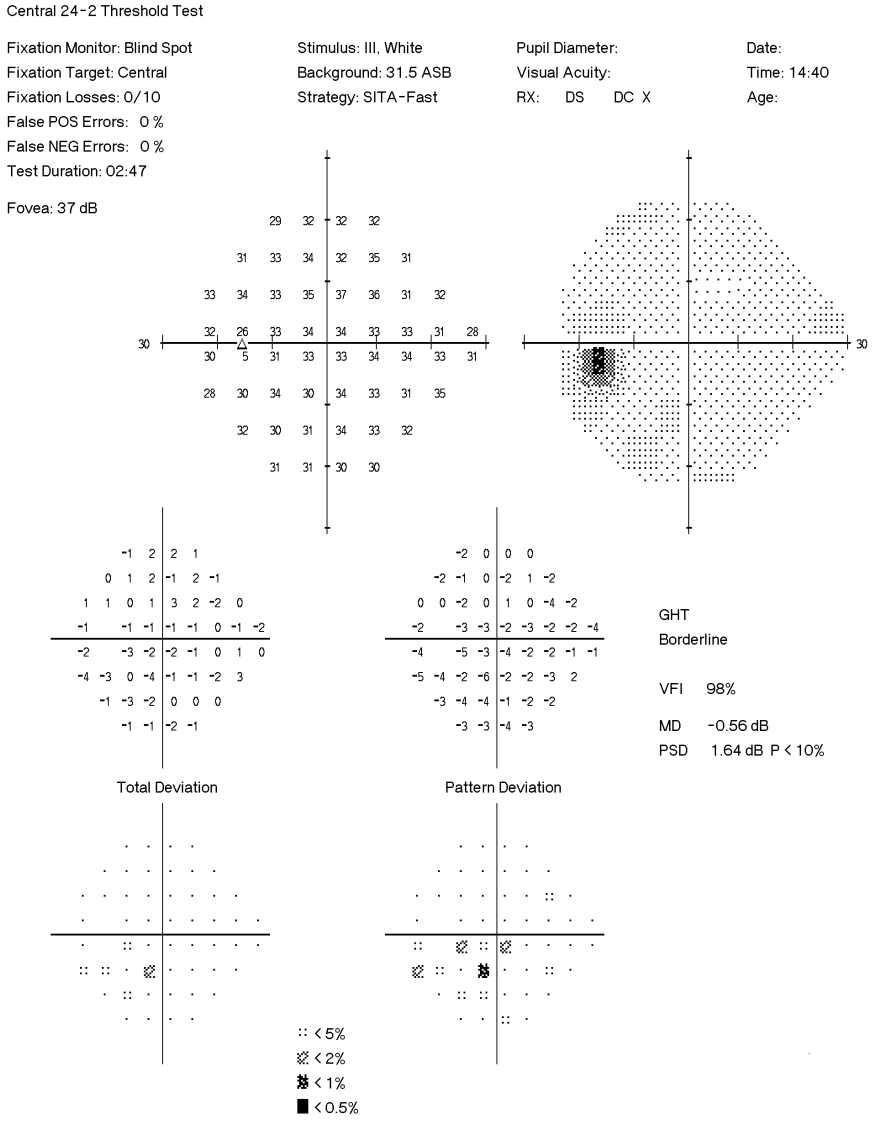


Figure 45. Subject without clear glaucomatous VF damage and reduced central visual acuity (0.46 LogMAR)

5.2.6 Comparison of SITA FAST and SITA standard algorithms

Nineteen subjects underwent assessment with both the SITA 24-2 FAST and the standard algorithms (testing one, rather than both eyes) as part of the repeat testing protocol (see study design, pg. 57). All subjects successfully completed both perimetric tests. Testing (including preparation time) with the standard algorithm had a mean duration of 8.6 minutes (SD = 2.1), significantly longer than the SITA FAST (p=0.004) (mean 6 minutes (SD 1.5)).

18/19 (94.7%) were rated with a good EBAR score using the SITA FAST, vs. 16/19 (84.2%) using the standard algorithm. Thus, the SITA FAST algorithm was more reliable than the standard algorithm (χ^2, p=0.018), though the sample size in this group was low.

Bland-Altman analysis between the standard and FAST algorithms showed no difference in MD (p=0.215) or PSD (p=0.316) values.

14/19 (73.7%) subjects rated difficulty of testing with SITA standard as 'OK', with 2 (10.5%) and 3 (15.8%) rating it as 'hard' and 'easy' respectively. SITA FAST was rated as 'OK' by 9 (47.4%) subjects, with the remaining 10 (52.6%) reporting testing as 'easy'. No child rated the standard algorithm to be easier than SITA FAST.

7/19 (36.8%) subjects reported finding no differences between the algorithms – when asked they reported "they're [the SITA FAST and standard algorithms] the same." 2 (10.5%) subjects reported finding the FAST algorithm to be noticeably shorter, and thus easier (less fatiguing). Five (26.3%) children reported a difference

in the brightness of stimuli between the tests, noting the FAST algorithm stimuli were brighter, or that the standard algorithm produced 'dimmer' stimuli.

5.2.7 Self-report of examination experience

Table 26 (below) shows subjects' ratings of test difficulty at their visit – i.e. using Humphrey SITA 24-2 FAST and combined Octopus G-TOP and kinetic perimetry (see methods, pg. 76). Very few (<5% in total) rated each test as 'hard' or 'very hard'.

Table 26. Participant reported test difficulty ratings for both perimeters

Subjective response	Humphrey perimetry (%)	Octopus perimetry (%)
Very Hard	1(1.6)	0 (0)
Hard	2 (3.1)	2 (3.2)
OK	39 (60.9)	28 (44.4)
Easy	19 (29.7)	24 (38.1)
Very Easy	3 (4.7)	9 (14.3)

A higher proportion of children rated Octopus perimetry as 'easy' or 'very easy' (52.4%) compared to Humphrey perimetry (32.8%).

Based on comments made by children on the test procedure/difficulty, 3/64 (4.7%) children reported that familiarity/experience with Humphrey assessments helped with testing. 26/63 (41.3%) children reported that Octopus perimetry was either fun/more interesting, or a novelty and expressed a general preference for the kinetic element of the combined test. 11/63 (17.5%) reported that the kinetic assessment allowed for more time to react to stimuli, and often commented that they could always see stimuli eventually (with centripetal movement), thus

providing a positive psychological impact of giving a 'correct' response. Some children (*n*=4 (6.3%)) found kinetic testing more challenging than static – but of these, 2 stated that they preferred a more challenging assessment.

5.3 Neuro-ophthalmic group (Group C)

5.3.1 Sample demographics

Between June 2013 and May 2015, 31 children were approached to take part in this phase of the study. 30/31 (96.8%) agreed to participate. Participant age and sex demographics are shown in Figure 46 (below). The mean age of subjects was 11.1 years (SD: 2.6) with 12 (40%) females. Participants were predominantly White (*n*=22 (73.3%)), with 3 Black, 4 Asian and 1 Mixed ethnicity child.

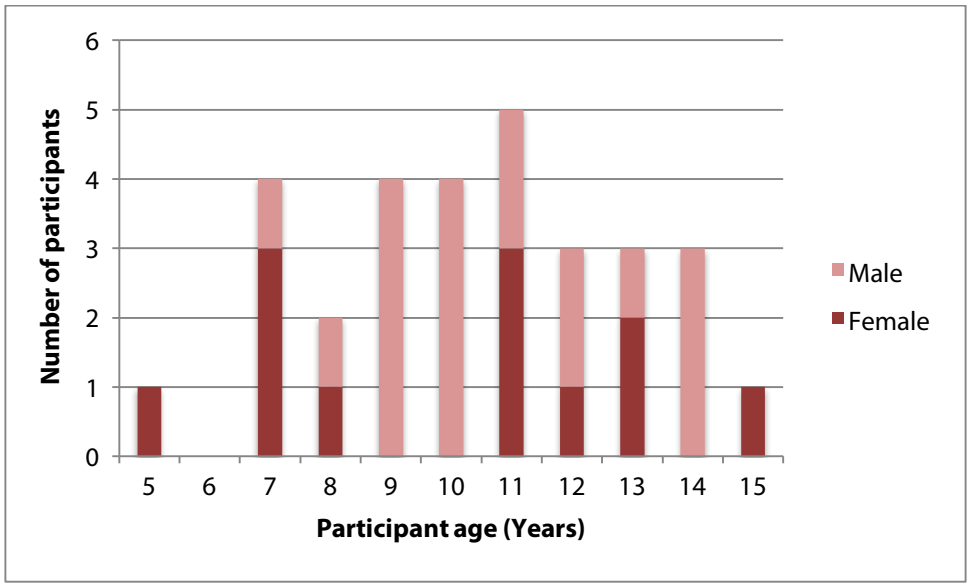


Figure 46. Group C (neuro-ophthalmic disease) sample demographics by age and sex (*n*=30)

Six (22.2%) subjects had no previous perimetric testing experience. 20 had prior experience ranging from 1 to 8 years (median of 2 years' experience (IQR: 1-3.5 years)), with a median of 1.25 tests (IQR: 1-2.1) per year.

Table 27 (below) lists ophthalmic diagnoses for all subjects in this sample, grouped by condition.

Table 27. Classification of neuro-ophthalmic diagnosis for participants (*n*=30)

Neuro-ophthalmic diagnosis
Chiari I malformation
Cervical meningocele with hydrocephalus and Chiari II malformation
Suprasellar epidermoid cyst
Suprasellar cyst. Hydrocephalus with VP shunt.
Epilepsy (lobectomy)
Langerhan's cell histiocytosis with lesions in the base of skull and orbits
Arachnoid cyst – tilted discs with bilateral peripupillary atrophy.
Bilateral discrete white matter lesions
Transverse myelitis with optic neuritis and disc pallor BIH
BIH and AML
IIH (x4)
Secondary IIH (post steroids)
Papilloedema
Pontine cavernoma
Pituitary stalk lesion
Glioma (Occipital lobe high grade)
Glioma (Optic nerve (x2))
Grade I ganglioglioma (left cerebellum). Posterior fossa craniotomy.
Medulloblastoma
Pilocytic brainstem astrocytoma with a paramacular scar
Posterior fossa astrocytoma (resected). L 4th NP
Craniopharyngioma treated with cyst decompression and photon therapy.
Craniopharyngioma treated with proton beam therapy
Craniopharyngioma (partially resected)

One subject (aged 10 years) became upset during their first perimetric test, and withdrew before completing their second test (Octopus). Goldmann data for this subject are presented where appropriate.

Median LogMAR acuity was 0.02 (IQR: -0.08, 0.12). Median spherical equivalent was 0.0D (IQR: 0.0, 0.375). Figure 47 (below) shows the distribution of refractive error in this study sample.

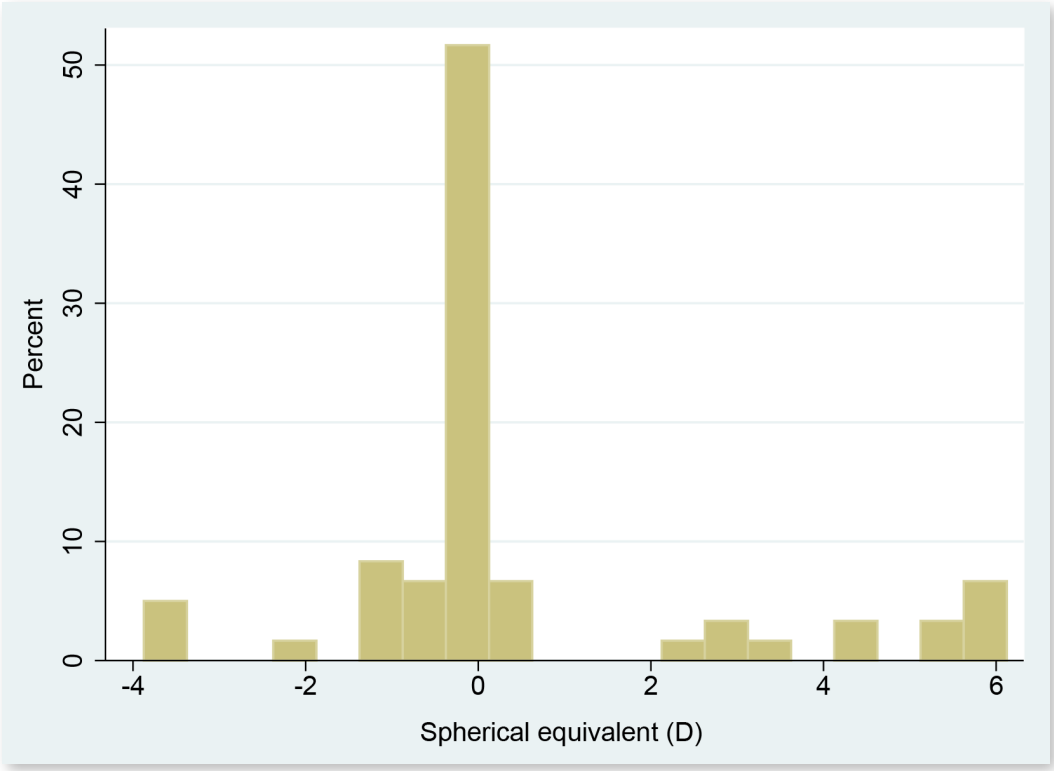


Figure 47. Spherical equivalent (D) of children with neuro-ophthalmic disease

5.3.2 Feasibility of perimetry

5.3.2.1 Test completion

27/30 subjects (90%) completed the Goldmann assessment. The 3 subjects that failed to complete assessments were unable to have their blind spot plotted. 22/30 (73.3%) completed the Octopus assessment (Table 28, below). Of these, 5 were unable to have their blind spot plotted, 1 failed to plot a KPRM, 1 abandoned testing and the final child was unable to proceed beyond Goldmann perimetry due to fatigue.

5.3.2.2 Test duration

Table 28 (below) summarises test duration for both perimeters, by age group.

Table 28. Test feasibility for Goldmann and Octopus perimetry – Group C (*n*=30)

Age group (years)	Sex		Number completing assessments (%)		Median test duration (min) (IQR)	
	Male	*Female*	*Goldmann*	*Octopus*	*Goldmann*	*Octopus*
5-7	1	4	4 (80)	3 (60)	16 (14-17)	16 (15-17)
8-11	11	4	14 (93.3)	10 (66.7)	18 (16-19)	17 (15-19)
12-15	6	4	9 (90)	8 (80)	17.5 (16-19)	18 (15-19)

** Test duration values include preparation and assessment tasks*

Test duration was not significantly different between the two perimeters (p=0.365), and did not change with age for Goldmann (p=0.939) or Octopus perimetry (p=0.127).

Two children required breaks during Goldmann perimetry. Of these, 1 child was upset after the first perimetric test (Goldmann) and was subsequently unable to

continue with the protocol (i.e. Octopus perimetry). The other child took a 6 minute break after Goldmann perimetry, and was still unable to complete testing with Octopus perimetry (reporting severe fatigue). No child required a break to complete Octopus perimetry.

5.3.3 Quality/Reliability of perimetry

The quality of each perimetric assessment was rated using the EBAR scoring system (categories of 'good', 'fair' or 'poor' quality), as shown in Figure 48 (below).

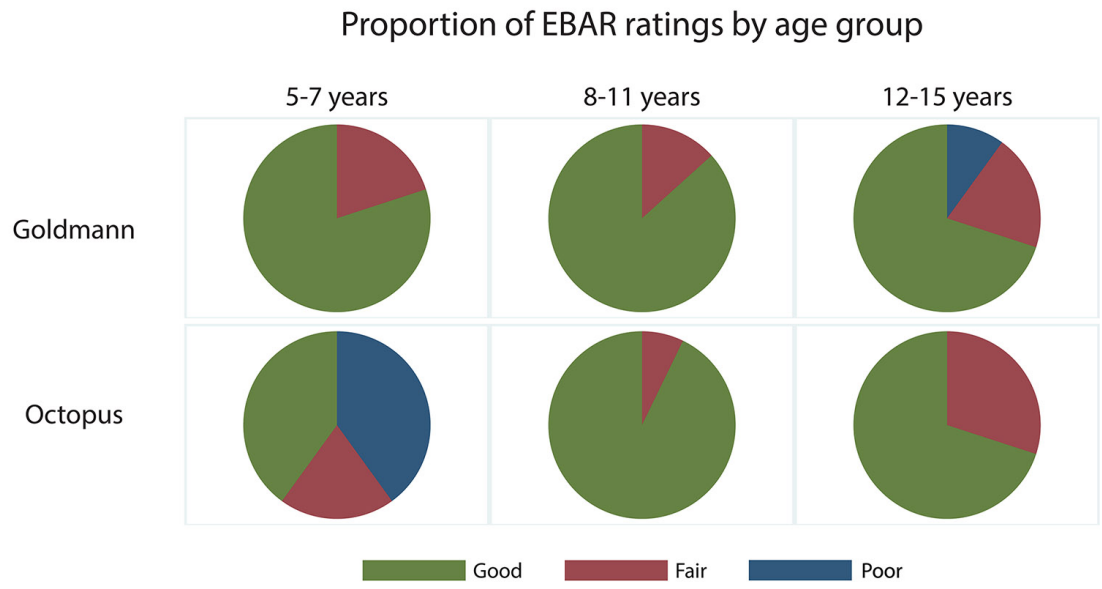


Figure 48. Proportion of EBAR (test quality) ratings per perimeter, by age groups

There was no change in reliability (measured with EBAR) with increasing age for Goldmann (p=0.388) or Octopus (p=0.129) perimetry. Children under 8 years demonstrate better reliability with Goldmann perimetry (80% good EBAR) than Octopus (40% good EBAR), yet there remained a proportion of children (>25%) over 12 years of age that could not perform a perimetric test to a 'good' standard – a trend not seen in children without VF loss (Group A – Figure 20, pg. 97).

One child had an unreliable blind spot assessment with Goldmann perim etry and 2 for Octopus. Thus in total, there were 4 and 7 either missing or unreliable blind spot plots for Goldmann and Octopus perimetry respectively. These do not include those with midline defects in whom it is not possible to plot a blind spot.

5.3.4 Self-report of examination experience

Table 29 (below) shows subjects' ratings of test difficulty at their visit.

Table 29. Participant reported test difficulty ratings for Goldmann and Octopus perimeters

Subjective response	Goldmann perimetry (%)	Octopus perimetry (%)
Very Hard	0 (0)	0 (0)
Hard	2 (7.4)	0 (0)
OK	11 (40.7)	14 (51.9)
Easy	7 (25.9)	10 (37.0)
Very Easy	7 (25.9)	3 (11.1)

Comments on the audible noise of Octopus stimulus presentation were made by 2/29 (6.9%) children. Both reported that the sound affected testing; one reporting that the noise provided warning of an impending stimulus, the other stating that it made the test harder.

Two children reported a preference for Goldmann perimetry, stating that the central fixation point was easier to see and an audible buzzer was better.

Eight preferred assessment with the Octopus describing that; the buzzer was more reliable/different, stimuli (*n*=3) and the central fixation point (*n*=2) were

easier to see, and the chinrest was more comfortable. Children also reported that they preferred a newer/computerised technique.

5.3.5 VF test outputs

Table 30 (below) shows classification scores (using the system reported in Table 11, pg. 89) for Goldmann and Octopus test outputs in those that achieved a 'good' quality rating for each test. An increasing score is indicative of greater visual field loss. No subject was classified with Grade 5 – the highest level of visual field loss.

Table 30. Comparison of Goldmann and Octopus classification scores ('good' EBAR only)

Goldmann classification score	Octopus classification score					Total
	0	**1**	**2**	**3**	**4**	
0	7	4	0	0	0	**11**
1	6	3	1	0	0	**10**
2	0	2	7	0	0	**9**
3	0	1	3	1	0	**5**
4	0	0	0	1	2	**3**
Total	**13**	**10**	**11**	**2**	**2**	**38**

** Shaded areas represent equivalent scores. N.B. Only subjects that have scores for each test are shown here.*

Goldmann and Octopus classification scores showed 'substantial' agreement (κ=0.62 (linear weighted), good EBAR results only). 11/18 (61.1%) results that do not agree have a lower Octopus score.

Bland-Altman analysis (shown in Figures 49-51 (mean difference (centre line) and upper/lower limits of agreement)), using tests rated as 'good quality', shows good

agreement between Goldmann and Octopus isopter areas for isopters I4e (p=0.814), I2e (p=0.450) and the blind spot plot (p=0.451). There was a mean difference of -463.2 deg^2 (95% CI: -773.3, -153.1) for isopter I4e, -505 deg^2 (-835.6, -174.3) for isopter I2e, and 16.6 deg^2 (3.7, 29.5) for the blind spot.

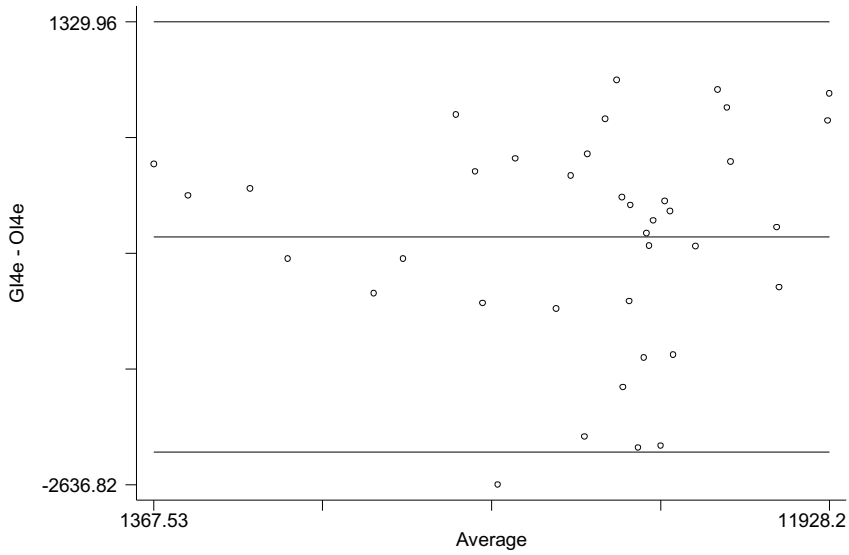


Figure 49. Bland-Altman plot of isopter I4e area, comparing Goldmann and Octopus perimeters

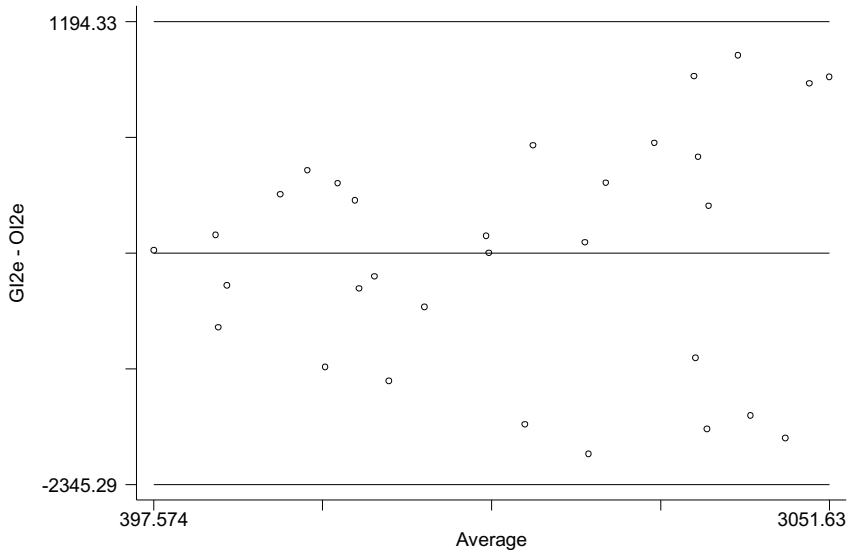


Figure 50. Bland-Altman plot of isopter I2e area, comparing Goldmann and Octopus perimeters

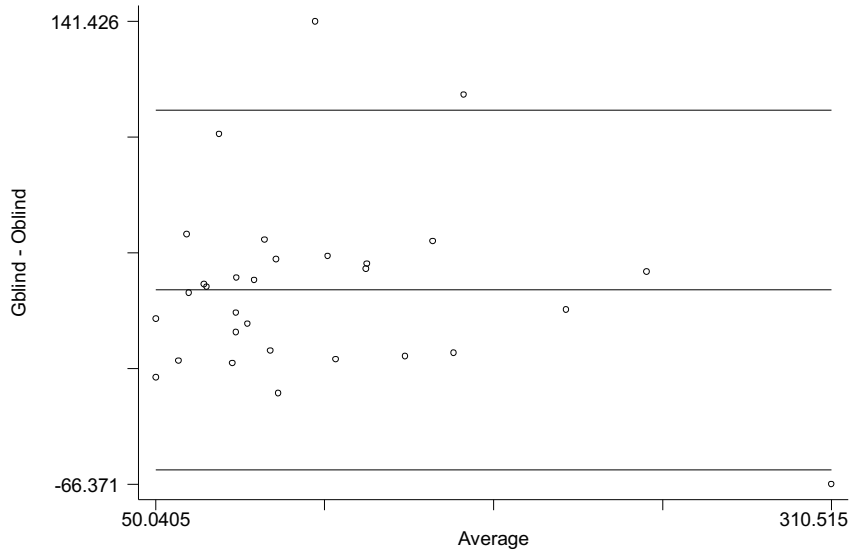


Figure 51. Bland-Altman plot of blind spot area, comparing Goldmann and Octopus perimeters

5.3.5.1 Blind spot size

Overall median blind spot size for good quality tests for Goldmann perimetry was 97.1 deg^2 (IQR: 80.8 to 134.4) and 76.2 deg^2 (IQR: 57.8 to 114.9) for Octopus perimetry. Table 31 (below) demonstrates the difference in blind spot size between those with classification scores of 0 and ≥1 for tests rated as 'good' quality.

Table 31. Blind spot size for classification scores of 0 or higher

	Goldmann classification score			**Octopus classification score**		
	Reference	**0**	**≥1**	**Reference**	**0**	**≥1**
Median blind spot size (deg^2) (IQR)	76.4 (61.4 to 94.7)	84.5 (72.6 to 94.3)	113.6 (86.2 to 147.7)	60.8 (41.9 to 80.6)	79 (68 to 97.5)	75.5 (53.9 to 135.5)

** Reference values are based on Group A normative data*

5.4 Between-group comparison

The following section draws comparisons between those data that are comparable for children in all 3 phases (control, glaucoma and neuro-ophthalmic disease). Table 32 (below) shows a comparison of test completion, duration and quality between phases, split by age groups.

From this, it is evident that, when compared to age-matched controls and those with glaucoma, children with neurological disease are less likely to be able to complete perimetric testing. Similarly, test reliability is lower, masking the improvement with increasing age seen in groups A and B.

Table 32. Comparison of test feasibility and reliability between subject groups

	Age group (years)	Testing group						
		Normative (control) (*n subjects* = 154)			Glaucoma (*n subjects* = 65)		Neuro-ophthalmic disease (*n subjects* = 30)	
		Goldmann kinetic	Octopus kinetic	Humphrey SITA 24-2 FAST	Humphrey static	Octopus combined	Goldmann	Octopus
Test completion (%)	**5-7**	94.5	84.9	100	100	100	80	60
	8-11	96.4	90.9	100	100	96	93.3	66.7
	12-15	100	96.2	100	100	100	90	80
Mean test duration* (minutes) (SD)	**5-7**	9.5 (1.9)	9.1 (1.7)	6.7 (1.2)	18 (3.1)	20.2 (4.8)	16.8 (3.7)	15.4 (5.4)
	8-11	9.0 (1.3)	8.7 (1.3)	5.4 (1.2)	13.1 (3.3)	16.3 (3.7)	17.7 (3.8)	16.9 (3.6)
	12-15	8.6 (1.1)	8 (0.9)	4.6 (0.7)	12.8 (2.8)	16.5 (2.9)	17.1 (2.1)	17 (3.4)
Test quality (% 'Good quality')	**5-7**	69.9	43.8	42.5	33.3	16.7	80	40
	8-11	87.3	76.4	74.6	76.9	64	86.7	92.9
	12-15	100	100	100	100	97.0	70	70

**Includes task preparation time*

5.4.1 Comparison of blind spot size between Groups A and C

The 'normal' (Group A) blind spot size for Goldmann perimetry was 76.4 deg^2 (IQR: 61.4 to 94.7) and 60.8 deg^2 (IQR: 41.9 to 80.6) for Octopus perimetry.

Children in Group C (neuro-ophthalmic group) demonstrated larger blind spots – with a median size of 97.1 deg^2 (IQR: 80.8 to 134.4) for Goldmann and 76.2 deg^2 (IQR: 57.8 to 114.9) for Octopus perimetry.

Importantly, in children without visual field defects 10.4% and 29.2% were unable to plot a reliable blind spot plot with Goldmann and Octopus perimetry respectively. This was similar for children with neuro-ophthalmic disease in whom 13.3% and 24.1% could not plot a reliable blind spot with Goldmann and Octopus perimetry respectively.

Chapter 6 Discussion

Strengths and limitations of the study and key findings are presented in this chapter. Findings comparing different approaches to perimetry in children with glaucoma and neuro-ophthalmic conditions are discussed in relation to their implications for practice and future research.

6.1 Strengths and limitations

To our knowledge, this study is the largest of its kind to date in children, and assessed multiple common perimetric tests, using clinically suitable protocols and robust analyses in children with and without ophthalmic disease. These techniques form an established part of adult ophthalmic clinical care, yet optimal approaches to perimetry in children are unknown.

Participation for the normative group was low (44.3%), but is at an expected level for recruitment in an 'unaffected' population. Our sample was large enough to generate reliable normative data, and the variability of findings can be used as a reference for power calculations in future studies using similar assessment protocols and analytical methods. Those that chose not to participate/non-responders were of a similar age/ethnic distribution to the sample and, with respect to these factors, did not induce a participation bias.

For future studies recruiting healthy controls, we would suggest that participation could be improved by using less time consuming protocols but at the cost of the ability to address as many research questions. If the participation rate cannot be improved, recruiting from multiple centres will help to reduce the burden of

recruitment on each centre, but requires research staff at each site. The issue of participation, potential selection bias, and burden of recruitment on centres is rarely addressed in paediatric ophthalmic literature, making comparisons difficult.

Participation rates for the glaucoma (82.9%) and neuro-ophthalmic groups (96.8%) were much higher, which is in line with expectations, as patient groups tend to have greater engagement than controls. The sampling strategy, combined with high participation, minimised potential sources of bias, maximising the generalisability of our findings to our target clinical population.

Potential sources of bias in the normative group, such as learning and fatigue were minimised by randomising test order. We included children without binocular functions/stereopsis to ensure the sample reflected the target population for visual field testing in a clinical setting and because prior evidence indicated that 'fellow' eyes in children with strabismus have normal visual fields.[51, 74] The present study was designed with an awareness of the issues surrounding data capture of subjective responses in children. Our pragmatic approach in the first phase of the study (group A) allowed us to generate normative data for three perimetric assessments, but meant we were unable to measure both eyes or assess repeatability in a single sitting. Other limitations include the reduction of sample size after the exclusion of tests that were not rated as having 'good' reliability, precluding analysis of Octopus perimetry using the quantile regression model in the 5-6 year age group. Nevertheless, this study is the largest systematic study of feasibility and reliability of perimetry in children without ophthalmic disease assessing three key approaches. It is also the largest to investigate the role

of perimetry in the diagnosis and management of childhood glaucoma and neuro-ophthalmic disease.

As with any study assessing subjective responses in children, our study was designed to capture as much relevant data in a single sitting, without reducing the data quality from fatigue, or inducing sampling bias by use of protocols that subjects/families would be unwilling to undertake i.e. those that last for half a day or longer.

Additional issues relating to children with visual field loss (i.e. those being monitored for active ophthalmic/neurological disease), relate to the fact that testing was performed with the gold-standard clinical measure first. This is likely to have caused fatigue effects in the second (comparator) test, with potential learning effects during the first test. However, modifying the design of the study would have impacted on standard patient care, and could have negatively impacted on study participation.

Our methods and novel analyses make it difficult to directly compare our results to the extant literature. However, our design, randomising where appropriate, and with an adequate sized sample allowed us to answer important clinical questions relating to the role of perimetry in the management of paediatric ophthalmic disease and generalise results to make suggestions for clinical protocols.

6.2 Feasibility of perimetry in children

The testing protocols used here are suitable for use in a clinical setting, combining short familiarisation tasks with short (optimised) algorithms/kinetic protocols. By careful positioning,[61] familiarising, and engaging the subject with the task,[138] we

were able to maximise the potential for a reliable result even in children as young as 5 years. Our data also demonstrated the limits for number of points plotted per isopter (in kinetic perimetry) for the first time.[45]

Subjects in the control group and those with glaucoma demonstrated very high test completion rates (>90%) with all perimeters. Most children were able to understand the test instructions, and sit in position at a perimeter for the duration of the assessment. For children with neuro-ophthalmic disease, the overall completion rate was 70% for Octopus perimetry (90% for Goldmann). The most common cause for failure to complete a kinetic assessment, across all groups, was an inability to successfully delineate a blind spot – an important measure for children with neuro-ophthalmic disease. We suggest semi-automated kinetic perimetry should be replaced with a fully manual technique (also available using Octopus perimetry) for plotting the blind spot, allowing finer control of stimulus presentation.

In children with glaucoma, poor visual acuity and fatigue were the only reasons recorded for a failure to complete assessments. Modifications for successful alignment at the perimeters were necessary for some of the youngest children, which have the potential to impact on test reliability. The Goldmann perimeter was the most flexible (with the greatest chinrest manouverability), and this is reflected in the better reliability ratings in the youngest children.

In children without VF loss, testing with static algorithms was shorter than detailed kinetic examinations using 2 isopters and a blind spot plot. Direct comparisons of our findings with prior studies are difficult, as prior studies have

used 12 test points (4 meridian – repeated twice), with a mean test duration of 5.1 minutes[43] or have tested along 8 meridian with one isopter (mean duration=11.06 min),[45] with considerable variation reported in test duration with similar protocols, highlighting the potential influence of examiner experience in manual perimetry. We used a highly detailed protocol yet the mean test duration for Goldmann perimetry was 9.2 minutes (SD=1.6) and 8.8 minutes (SD=1.5) for Octopus perimetry, indicating that detail and quality can be achieved with a child-appropriate test duration.

As expected, a combined static/kinetic assessment in children with glaucoma takes longer to perform than static perimetry alone. For combined perimetry, changes in test quality were not associated with duration of assessments (unlike children without VF defects), and this is likely due to shorter kinetic elements in those with poor quality tests counteracting the effects of a longer static element. Fewer breaks overall were required to complete combined assessments, indicating that children respond well to short periods of testing. Thus, adapting testing by accommodating rest breaks in protocols may help to improve test reliability, especially for children with severely damaged VF's, in whom performing static perimetry is a lengthy process.

The lack of relationship between subjects' perceived test difficulty and test reliability underlines the importance of encouraging children through tasks they perceive as difficult. Static perimetry (SITA 24-2 FAST) was the shortest test used here, yet had the poorest reliability in young children and participant responses identified the intensity of the task as a potential cause of this.

In children with glaucoma, the novel, engaging experience of a kinetic assessment was positively received. Children also commented on a preference for centripetal stimuli, as they were assured to see the stimulus eventually, and thus did not feel they ever gave a negative or incorrect response. This is also reflected in adult literature, where those with advanced glaucoma show a preference for kinetic perimetry, and better test-retest reliability.[111]

In children who find it difficult to cooperate, have difficulty concentrating for long periods, or have advanced visual field loss, kinetic perimetry may offer a suitable alternative to static assessment. When choosing a perimetric test, the impact of subjective experience should be carefully considered, as it has the potential to affect not only the quality of a single test, but may impact on the performance of testing in future.

6.2.1 Other factors affecting test feasibility

Fatigue is known to impact on test reliability and outcomes.[139] For static perimetry (with threshold algorithms) this affects the accuracy of the entire test, whereas points plotted by kinetic perimetry before the onset of fatigue will still provide useful data. 15% of the cohort with neuro-ophthalmic disease could not complete the study protocol – and this was attributed to severe fatigue.

Thus, in a child who tires quickly, or struggles with intensive testing, plotting a baseline kinetic field can give valuable information on visual field sensitivity that cannot be achieved by static techniques. Our data suggest it is possible to find balance between performing the test quickly (minimising fatigue) and ensuring children do not feel overwhelmed by the task.

Other differences between perimeters are important factors to consider when testing children i.e. the ease of positioning child subjects, and the audible clues given by the Octopus perimeter on kinetic stimulus presentation.

Our findings show that, with age appropriate instructions and test protocols, visual field testing using commonly available perimeters is highly feasible in children as young as 5 years of age. Although visual field damage and acuity are not necessarily correlated (e.g. in glaucoma), it is not possible to successfully assess those with severely reduced central acuity. Children with glaucoma, as included in the present study, routinely undergo perimetry from 10 years of age, with tests generally performed annually. Starting assessments at an earlier age could lead to an accurate 'baseline' visual field earlier in life (mitigating potential learning effects); with a greater ability to monitor change over time.

The choice of perimetric technique should be informed by the clinical context of individual cases, balancing the need for detailed examinations against the ability of a child to perform an assessment reliably.

The quality of perimetric assessments (i.e. test reliability) improves with age, and accurate interpretation of findings relies on effective measurement and documentation of test reliability, as discussed in the next section.

6.3 Reliability of perimetry in children

Two novel measures of reliability were developed for use in this study. They were designed to provide complementary information, and address the lack of standardised reporting of VF test quality in children. The Examiner Based Assessment of Reliability (EBAR) is a qualitative score factoring for behaviour that

affects test quality, such as concentration, co-operation, fatigue, and fixation (Table 5, pg. 63). The second measure, the Kinetic Perimetry Reliability Measure (KPRM), is a quantitative score, also providing a visual representation of within-test variability (see methods, pg. 67).

6.3.1.1 The Examiner Based Assessment of Reliability (EBAR)

Studies of static perimetry in adults commonly use automated indices (false positives, false negatives and fixation losses) to describe test reliability. No evidence exists regarding their effectiveness in classifying test reliability in children and equivalent measures are not available for kinetic perimetry.

For children without VF loss (group A), a combined reliability index (comprised of false positives and fixation losses) showed poor agreement with EBAR scores. This lack of agreement with fixation losses could be attributed to the way the Humphrey perimeter tracks fixation (Heijl-Krakau method). Other perimetric techniques, such as fixation monitoring on the Octopus perimeter or micro-perimetry (where stimuli are not presented unless fixation is steady) offer better fixation control, but are disruptive to the test process in those with poor fixation and are thus of limited value in the assessment of children. Our data suggest that false positives alone (an attribute that can't be easily judged by EBAR) are a better measure of test reliability and are thus able to add complementary information to an EBAR score.

Given that currently, there are no standardised methods for scoring test quality in kinetic perimetry – for adults or children, our development and use of a new qualitative measure (EBAR) is a useful innovation and also provides information

complementary to automated indices from static perimetry. EBAR can also be compared to childrens' perception of test difficulty.

6.3.1.2 The Kinetic Perimetry Reliability Measure (KPRM)

An increasing KPRM score is indicative of poorer test reliability (Results, pg. 98), thus providing a novel indicator of reliability for kinetic perimetry. The KPRM is simple to implement and interpret and can be used in children as young as 5 years.

Median values are less susceptible to the effects of outliers. By defining the KPRM score as the median of four values it is less influenced by a single large/small KPRM point, providing a more robust reflection of test repeatability. The score is presented as a summary value, yet the individual points that produce the KPRM score hold a descriptive value. They are able to suggest fatigue (all points within the original isopter) or learning effects (consistent plots outside the original isopter (Figure 21b, pg. 100), and can provide information on variability of responses within each quadrant. Notably, a visible difference in isopter appearance is evident with decreasing test quality (Figure 21a-c, pg. 100), emphasising that, in these normal subjects, VF tests of fair/poor reliability struggle to represent a subjects' true visual field.

Our programme of research focuses on children, i.e. the population in whom there is a higher likelihood of unreliable results. However our sample size limited the ability to define expected KPRM values for different test quality levels and precluded our ability to perform analysis using complex statistical methods/models. Nonetheless, higher KPRM scores are associated with poorer

test quality, demonstrating that reproducibility is poorer with reducing overall test reliability. For those in whom EBAR and KPRM ratings were discordant, additional examiner comments could explain the fluctuation in test quality.

Currently, no similar measures of reliability of kinetic perimetry exist against which we can compare the KPRM approach. We describe a concise method of quantifying within-test variability that could be used in future studies as a proxy to assess perimetric test reliability.

When implemented alongside our examiner rating of test quality (EBAR), the KPRM is able to provide information useful in interpreting serial VFs over a number of visits. The KPRM can describe small fluctuations in test reliability that cannot be captured solely by the use of the EBAR.

6.3.2 Test reliability in children with and without VF loss

Reliability of perimetry improved with age for children without VF loss and glaucoma, but over 25% of children age >12 years with neuro-ophthalmic disease still struggled to perform a good quality test. For children without VF loss, and those with neuro-ophthalmic disease (Groups A and C respectively), Goldmann perimetry was the most reliable technique in children under 8 years of age. In children under 10 years of age, with glaucoma, the Humphrey SITA 24-2 FAST was the most reliable technique, compared to a combined static/kinetic technique.

In older children (all subject groups) all perimetric techniques were equally reliable. Thus, for a young child without glaucoma, assessment with Goldmann perimetry is the approach most likely to be capable of accurately measuring visual field sensitivity and those with glaucoma should be assessed with a fast static

algorithm. After 10 years of age, the choice of perimetric test should largely be informed by the clinical context of individual cases.

A recent report on Octopus perimetry in children (controls) using a detailed test protocol has shown that, as children struggled to plot a blind spot, only 64% of those aged 10-12 years could plot reliable fields.[35] This contrasts with our study, in which children demonstrated better reliability. This may reflect the more nuanced assessment of reliability we used, compared to the pre-defined metrics others have used (generally based upon standards used in adult populations), but could also reflect variation in assessment protocols between studies.

Our data suggest that the SITA FAST algorithm yields better reliability than the SITA standard, but the difference is small and warrants further investigation with a larger sample. Further comparisons of SITA FAST and Standard are made in section 6.6 (pg. 163). There are very few studies against which we can compare directly our data on VF reliability in children with glaucoma, as many prior studies have used different techniques or failed to report test reliability, instead focussing on test feasibility alone.[107, 108, 140, 141] Thus, the findings presented here provide the first large-scale investigation of perimetric test feasibility and reliability in children with glaucoma.

Our data on children with neuro-ophthalmic disease reflect the heterogeneity of this group of conditions. These were the only children to not demonstrate a clear improvement in test reliability with age, and this likely reflects the heterogeneity of the sample and effect of neurological disease on childhood development.

6.3.3 Summary

We suggest formal perimetry should be attempted in children over 5 years of age with suspected VF loss due to glaucoma or neuro-ophthalmic disease (Table 33, pg. 170). The reliability of these assessments can be documented using the EBAR scoring system we have developed, so that judgements can be made as to whether test results are likely to reflect true visual field sensitivity. The sole use of automated reliability measures for Humphrey static perimetry may lead to potentially useful results being disregarded and our data suggest false positive data can be combined with an EBAR score to better grade the tests reliability. For kinetic perimetry, we recommend the routine implementation of the KPRM alongside EBAR when assessing children.

6.4 Repeatability of perimetry in children

Repeatable visual field tests are considered to be reliable assessments, yet visual field loss affects the repeatability of assessments, even in reliable observers. Our sample of children without visual field loss, returning for repeat assessment, was too small to allow assessment of repeatability in depth. However, our data from those children with reliable assessments indicate repeatable test results. In adults, studies have shown that learning effects can persist for 5 years (when tested annually).[142] Surprisingly, neither we or others[35] have found clear evidence of a significant 'learning effect'. However, as it would be reasonable to expect some learning effects, especially with younger children and differentially in those with field defects as opposed to those with normal fields, this issue, as well as test-retest variability, requires further investigation.

The evidence base on repeatability remains incomplete and further investigation is necessary to assess how small but clinically significant changes in visual fields in children over time can be ruled in or out.

6.5 Development of visual fields in childhood

Our findings show that for children without ophthalmic disease (using Goldmann perimetry), the mean isopter area for isopter IIII4e was 17.8% larger, isopter I4e was 11.2% larger and isopter I2e was 63.1% larger in 15 year olds, compared to 5 year olds, a large change in VF areas over this 10 year range. This translates into a visible change in isopter appearance between the youngest and oldest subjects (Figure 31A to B, pg. 113), but with overlapping confidence estimates between age groups. It is critical to note the inner 2.5% quantile line increases in size with age. Thus, previously 'normal' values in young children are no longer 'normal' as age increases. Most of the developmental change occurs in the temporal and infero-temporal field, with a small increase nasal field size.

It is difficult to directly compare our kinetic data to the extant literature reporting VF size in children, as prior research involved assessments along fewer meridians, using large stimuli (V4e) only,[43, 45] or had a small sample and analysed with parametric methods.[46] However visual inspection does show that our results in the oldest children are broadly similar to the results of Egge[36] in 14-15 year olds (*n*=68, Goldmann perimetry) albeit with a slightly smaller nasal field in our study, but similar confidence estimates.

For Octopus perimetry, normative isopters have been modelled in adults using parametric methods and are therefore not comparable with data presented here.

We have produced area data for Octopus perimetry, and elected not to correct for reaction-time (RT) as children can demonstrate variable RT's through the course of a single test. The use of spline versus straight points also affects generalisability, and thus our results are not directly comparable with others.[35] Spline models describe changes of isopter values in relation to isopter area by fitting a nonparametric smooth function using curved lines. The use of linear models in our study, using straight as opposed to curved lines when estimating isopter area, affects the comparability of these results – yet provides the most robust representation of kinetic isopter distribution to date.

Direct comparisons of normative VF area outputs between Goldmann and Octopus perimeters show no significant differences, yet isopter shape appears to differ slightly (Figure 35-Figure 36, pg. 117). This underlies the importance of generating normative data specific to perimeters, rather than inferring results from similar specification machines, which is particularly important in light of the recent development of kinetic perimeters to replace Goldmann perimeters.

Humphrey MD values are a commonly used metric in the summary of visual field data in children. This study is the first to report normative SITA FAST values in children. Our findings show MD values to be age dependent and their interpretation should therefore take into account the age of the subject. Children under 10 years of age should not be expected to have adult visual field sensitivity levels (Table 17, pg. 119). Between 10 and 12 years, there is a good likelihood of achieving adult-like results (MD > -2 dB) and children >12 years should be expected to achieve adult sensitivity levels routinely.

Our findings provide normative, age-appropriate VF values in children, to serve as the basis for interpretation of visual field test results in children with ophthalmic disease.[143] They provide a means of bridging the gap in normative data for Goldmann,[36, 37] Octopus[38] and Humphrey[26] perimetry. We provide evidence for linear visual field growth (size) during childhood (between 5 and 15 years) as measured with kinetic perimetry (both Goldmann and Octopus), whilst visual field sensitivity, as assessed by static perimetry, (Humphrey SITA) reach adult levels at 12 years of age. We suggest that interpretation of perimetric findings should be based on knowledge of the normal range of area/size or sensitivity reported here. For example, when monitoring progressive visual field loss longitudinally in young children, a failure to demonstrate larger/more sensitive visual fields over a number of years may indicate loss of visual field function or arrested development, rather than stability.

6.6 Comparison of perimetric techniques in children with glaucoma

Our sample included experienced and non-experienced subjects, though most had already undergone routine annual perimetric assessment. It also included a high proportion of myopic subjects and a small proportion of aphakic children. Thus our sample reflects the population served by specialist childhood glaucoma centres, allowing us to generalise our findings to most children with glaucoma.

As discussed above, combined static/kinetic perimetry is as feasible as static perimetry alone and children require fewer breaks to perform a combined assessment. However, the reliability of combined tests is poorer in younger subjects. This is likely due to a longer overall test duration, though fatigue induced

through systematic bias (test order) is also a likely factor. Our data suggest that attempting a longer combined protocol is unlikely to be sufficiently useful in children under 10 years.

Static and kinetic perimetry in unaffected eyes of children with glaucoma exhibit normal VF sensitivity, indicating VF testing in eyes without VF loss shows good specificity. Thus, perimetry in unaffected eyes of children with glaucoma holds potential value by allowing these eyes to serve as 'controls' within individuals – providing information on underlying longitudinal developmental changes.

Humphrey and Octopus MD values show good agreement for values >-6, but in those with severe loss, Humphrey MD values are generally larger. Thus care should be taken when interpreting values from different perimeters. In particular, where possible, the same perimeter and algorithm should be used to monitor for change over time. As of yet, there is no literature available comparing Humphrey and Octopus perimetry over time in children with glaucoma.

Our data comparing SITA FAST and Standard algorithms did not show a meaningful difference in reliability between techniques. The algorithms are known to have equivalent precision for detecting progressive loss,[144] and thus we suggest, if testing is started at a very early age, the shorter algorithm be used in children.

Our data describe, for the first time, the relationship between static and kinetic perimetry in childhood glaucoma. They suggest that static perimetry (either using Humphrey or Octopus) is most likely to detect early glaucomatous VF loss, and should be performed as the initial VF assessment, especially in younger children.

Octopus static perimetry using the G-TOP algorithm potentially identifies milder VF loss than the SITA 24-2 FAST algorithm, but longitudinal studies of VF progression are required to confirm whether this translates to earlier detection of VF loss. Kinetic perimetry is capable of detecting mild defects but, in some instances, is not as sensitive as static perimetry.

The value of kinetic perimetry lies in the assessment of children with moderate/severe VF loss, allowing the full extent of the field to be assessed, i.e. sensitivity outside 30° of eccentricity (allowing detection of residual 'islands' of visual field sensitivity), a feature not possible with static perimetry alone. A moderate proportion of children in our sample with severe central defects demonstrated large areas of sensitivity outside 30°, and we suggest kinetic perimetry is performed for every child with moderate/severe glaucoma, mapping the full extent of the visual field. The kinetic assessment can be performed at a separate sitting for those too young to perform combined perimetry.

6.6.1.1 Summary

The choice of perimetric test should reflect the clinical features of individual cases. For example, where children exhibit reduced visual acuity and severely impaired central visual fields (measured by static perimetry), we advocate the use of kinetic perimetry to map the full visual field extent. Children with limited co-operation should be assessed with the least demanding test available.

6.7 Comparison of perimetric techniques in children with neuro-ophthalmic disease

Our sample contained many subjects who were highly experienced with Goldmann perimetry, having commonly performed more than one perimetric test a year. Kinetic perimetry with the Octopus utilises the same testing mechanism, with a slightly different test experience. Children were quick to note this, though were less affected by the sound of the perimeter than controls (11% vs. 6.9%). In general, children preferred assessment with Octopus perimetry, though as noted in the 'controls' (Group A), favourable perception of a test does not relate to a better test quality.

Both tests were capable of detecting neuro-ophthalmic defects, yet 50% of tests did not have a matching classification score. Of these only 1/38 (2.6%) result had a disagreement of >1 classification scoring unit. However, for Goldmann results classified as ≥2, discordant results always resulted in a lower Octopus classification score, indicating that Octopus perimetry may slightly underestimate the most severe visual field defects. This again underlines the importance of consistency in testing – ensuring that children undergo similar test protocols on the same perimeter at each visit. The use of differing perimeters in the management of these children, whilst discouraged, is at times unavoidable. Our data suggest that in these instances perimetric findings should be interpreted with extreme care.

The Octopus perimeter represents a suitable alternative to the current gold-standard Goldmann in children aged 8 years and over. It is possible that test order effects had greater impact on test quality in children <8 years, and thus, if

Goldmann perimetry is unavailable, Octopus perimetry should still be considered in these children.

6.8 Perimetry in the management of paediatric ophthalmic disease

We have shown that in children with normal visual fields (i.e. fellow, or healthy eyes with good acuity), good quality perimetry is feasible in those as young as 5 years, although the prospects of achieving a reliable test improve with increasing age. Goldmann perimetry is the most reliable form of testing up to 9 years of age, but there appear to be no differences in test quality between different test strategies above this age. Good quality tests are reproducible on repeat testing. Older children are able to plot more detailed kinetic assessments, allowing for better delineation of isopter shape. Size/area and sensitivity of normal visual fields increases with age and interpretation of findings should account for developmental changes over time.

For those children where formal perimetry is not possible, child-specific novel assessments have been suggested. These consist of supra-threshold tests using eye-tracking,[54] or using modified perimeters.[52] Other techniques use game-based[145] or behavioural engagement.[146] These allow for a degree of quantification, but many of these require specialist equipment and are likely to only be performed in specialist centres.

From our data, it is evident that IOP is not sufficiently well associated with VF sensitivity in children with glaucoma for it to be considered as a proxy measure or a predictor. VA can be associated with extent of VF loss, but there is a proportion of children in whom this relationship is not evident. Thus, testing acuity cannot

serve as a direct proxy for monitoring visual field function. Perimetry is a valuable diagnostic tool, but as with any other test, it is only one facet of a clinical examination, and care should be taken not to over/under-value individual test results.[147]

In those with glaucoma, simple, fast static algorithms are the most reliable tests in children under 10 years of age. At this age, reliability is more dependent on the maturity/development of the individual child. Older children are able to tolerate more comprehensive testing, either using a longer static algorithm, or a combined static/kinetic technique. Static perimetry is quicker in those with more reliable responses and less damaged fields. Kinetic testing allows for quantification of sensitivity in the far periphery, and is necessary for those with severe VF loss.[148] Our findings, when combined with previous studies, suggest that VF testing in childhood glaucoma can and should be started from a young age to allow children to accustomise to testing, and mitigate learning effects. The choice of technique employed is dependent upon a child's clinical features. Those with minimal or mild loss may be assessed by static perimetry alone, whereas children with moderate/severe loss should have their assessment complemented by a kinetic approach from 10 years of age.

Our sample, drawn from children attending Great Ormond Street and Moorfields Eye Hospital, show that in current practice it is common for children to undergo annual perimetric testing. As such, if utilising kinetic perimetry, clinicians face decisions regarding increasing test frequency (alternating static and kinetic testing) or having longer tests per visit, balancing the potential for fatigue influencing reliability.

6.9 Perimetric guidance

The aim of this thesis (pg. 56) was to develop optimal strategies for the assessment of visual fields in children with glaucoma and neuro-ophthalmic disease. The section below (Table 33) summarises key findings from all groups of children to make recommendations for clinical practice.

Table 33. Recommended procedures for children with glaucoma and neuro-ophthalmic disease

<table>
<tr><th rowspan="2">Condition</th><th rowspan="2"></th><th colspan="11">Age (years)</th><th rowspan="2"></th></tr>
<tr><th>5</th><th>6</th><th>7</th><th>8</th><th>9</th><th>10</th><th>11</th><th>12</th><th>13</th><th>14</th><th>15</th></tr>
<tr><td rowspan="3">Glaucoma</td><td>All children</td><td colspan="11">Children should have reliability assessed using the EBAR scoring system. The use of fixation losses as a reliability index could cause potentially useful results to be disregarded, and thus should be interpreted with caution. KPRM should be undertaken in those tested with a kinetic isopter.</td><td rowspan="4">Interpretation of findings should be perimeter specific and account for age-related changes in visual field development.</td></tr>
<tr><td>VA better than 0.2 LogMAR</td><td colspan="6">Assess routinely using static perimetry only (Humphrey or Octopus perimetry)</td><td colspan="5">Assess routinely using combined static/kinetic perimetry</td></tr>
<tr><td>VA worse than 0.2 LogMAR</td><td colspan="11">Assess routinely using static perimetry (Humphrey or Octopus perimetry) with a baseline kinetic isopter plot. Repeat kinetic perimetry if there are significant changes in central field sensitivity.</td></tr>
<tr><td rowspan="2">Neuro-ophthalmic disease</td><td rowspan="2">All children</td><td colspan="11">Children should have reliability assessed using the EBAR and KPRM scoring systems.</td></tr>
<tr><td colspan="3">Assess with Goldmann perimetry (kinetic) using 2 isopters and a blind spot plot.</td><td colspan="8">Assess with either Goldmann or Octopus kinetic perimetry using 2 isopters and a blind spot plot. Avoid changing perimeter whilst monitoring visual field defects.</td></tr>
</table>

6.10 Perimetric Standard Operating Procedures (SOPs)

Perimetric SOPs have been developed and are shown in full in section 9.8.4 (pg. 378), incorporating novel findings from the OPTIC study with extant literature.

These SOPs require detailed evaluation from an expert panel to form a consensus approach, so that recommendations can be made to incorporate perimetric guidance into current clinical guidelines. In particular, the findings here relating to children with glaucoma and neuro-ophthalmic disease address gaps within current guidelines published by the WGA and RCPCH.

Chapter 7 Future work

The research reported in this thesis has advanced understanding of testing visual fields in children, reporting the feasibility of testing and investigating methods for assessing test reliability. The findings highlight the differences in testing between adults and children, demonstrating that it is not sufficient to simply apply evidence gained from adult literature to children. For example, it is evident that the sole use of automated reliability measures in judging test reliability is inappropriate in children, yet the static test algorithms developed for adults appear capable of detecting visual field defects in children with glaucoma. Thus, to provide information on the role of perimetry in the management of children with ophthalmic disease, future research should focus on recruiting children with the specific ophthalmic disease in question.

SOPs were developed from this study and, as reported earlier, further work is necessary (and planned) to develop these to be used in clinical practice and to inform future clinical guidelines.

Formal perimetry (as opposed to novel, game-based approaches such as SVOP) is available to clinicians in a hospital setting, and can be used to monitor visual fields throughout a person's life. As such, findings in childhood provide a 'baseline' that is potentially still relevant decades later. The section below will identify remaining gaps within the literature and set out a 'pathway' to develop greater understanding of the role of formal perimetry in the management of childhood ophthalmic disease, with an understanding of the lifelong care many children need.

Our investigations were performed with an understanding of the change in available perimeters in clinics. Whilst Goldmann perimetry remains the widely used clinical gold-standard, other techniques investigated here are feasible, but as of yet, not as reliable in young children. The emerging availability of 'third-party' perimeters (from Takagi and Inami), replicating Goldmann standards, have not yet been sufficiently explored within the literature to advise their use in children. This paucity of evidence, combined with the potential for failure of existing Goldmann apparatus leaves a potential compromise in patient care and thus there is a need for future research to prioritise available (rather than novel) techniques – namely an investigation of the apparent 'like-for-like' replacements offered by Takagi and Inami.

Further research should then explore the role of perimetry as a tool for monitoring disease progression. Currently, there is no consensus on the best method for tracking progressive visual field loss in adult glaucoma, extending to a lack of agreement on which algorithm to use, the best statistical method (pointwise, global etc.) and frequency of testing required to detect change. Given the lack of consensus over tracking progression in adults, there is limited evidence upon which inferences can be made and applied to children, and it is uncertain as to whether it would appropriate to do so. Tracking disease progression in children is further complicated by a lack of understanding of the effect of an insult to a developing visual system, which could give rise to trajectories of progressive visual loss not seen in adults.

For children with glaucoma, there is also a need to affirm known features of adult glaucoma, namely; to assess whether test results (visual field sensitivities) are more variable in severely damaged fields, define the number of serial tests needed to confirm progression, and investigate structure/function relationships – in particular, explore the relationship between perimetric findings, RNFL reflectance intensity and OCT findings/sites of damage.

Once there is a clearer understanding of the way in which glaucomatous field loss progresses in childhood glaucoma, it will be possible to create new tests to be applied to children currently too young to be reliably assessed. These new tests can be targeted to detect loss in known susceptible areas of the field, thus reducing the number of required test points, with awareness that not all loss can be detected without a standard 'grid' pattern. These tests will have limited value in defining a 'baseline' visual field sensitivity that can be tracked across the life course, but even with a small applicable age range, and limited long-term value, a novel algorithm could provide information on VF sensitivity in a group of children in whom it is currently not possible to obtain meaningful results. Any adaptations of conventional static algorithms would need to assess the optimal balance between the number/location of central static test points and test duration – reducing the number of test points, but maintaining the accuracy of testing at each point. As such, techniques to shorten test duration such as TOP (which relies on scores from nearby anatomical locations to infer sensitivity at adjacent points) may not be suitable, but a standard staircase method could be successful.

Using simplified static strategies from a younger age also has the potential to familiarise children with perimetric procedures, improving reliability later in childhood. This contrasts with current attempts to measure visual fields in children, which focus on supra-threshold stimuli and use eye-tracking technology to detect shifts in fixation – a behaviour that is actively suppressed during conventional perimetry.

Our data on children with neuro-ophthalmic disease highlight the difficulty in testing a challenging group of unwell children. Given the limited ability of these children, future work should examine the ability of each element of kinetic testing to detect neuro-ophthalmic defects. For example, in a child who struggles to perform kinetic perimetry using 2 isopters (far and mid-peripheral stimuli) with plotting of the blind spot, an investigation of which elements hold the greatest potential to detect defects, and monitor for progressive loss could allow clinicians to use limited test points to assess the visual field. Adapting protocols for a select group of children in this way should be performed with an understanding of the types of defect that could be potentially missed.

For children with neuro-ophthalmic disease, there is a lack of understanding of normal levels of 'noise' between test results, the number of tests required before having definitive perimetric evidence of progression and what constitutes a clinically significant change in visual field sensitivity. Addressing these questions will help to determine the intrinsic value of perimetric results in the clinical management of childhood neuro-ophthalmic disease i.e. at what level does a perimetric test result influence clinical decisions? A retrospective review of

perimetric findings, matching changes in visual field sensitivity with changes in findings from imaging and other clinical features, is key to addressing this question.

Finally, it is necessary to develop clinical tools to aid tracking progression with kinetic perimetry (similar to those that exist for static perimetry). Our newly developed R package is the first step in this process – providing a template for organising test responses into matrices suitable for analysis. Further work is necessary to develop progression-tracking measures. For example, automated tracking of changes in isopter extent per quadrant and reporting change in total isopter area are useful clinical tools that need to be automated, providing summary scores without extensive user input.

Combining the findings here with the future work outlined above would allow for greater understanding of how to measure visual fields in children, the role of perimetry in tracking visual field loss, and the way in which these can contribute to clinical care. Once this evidence is present, it will be necessary to update current guidelines, describing accurately the role of perimetry in the management of children with glaucoma and neuro-ophthalmic disease.

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Chapter 9 Appendices

9.1 Appendix I - Systematic review search terms

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(("visual fields"[MeSH Terms] OR ("visual"[All Fields] AND "fields"[All
Fields]) OR "visual fields"[All Fields] OR ("visual"[All Fields] AND
"field"[All Fields]) OR "visual field"[All Fields]) AND ("visual field
tests"[MeSH Terms] OR ("visual"[All Fields] AND "field"[All Fields] AND
"tests"[All Fields]) OR "visual field tests"[All Fields] OR "perimetry"[All
Fields])) AND (child[All Fields] OR child'[All Fields] OR child''[All
Fields]
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("Childhood"[Journal] OR "childhood"[All Fields]) AND ("glaucoma"[MeSH
Terms] OR "glaucoma"[All Fields])
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("Childhood"[Journal] OR "childhood"[All Fields]) AND
("Neuroophthalmology"[Journal] OR ("neuro"[All Fields] AND
"ophthalmology"[All Fields]) OR "neuro ophthalmology"[All Fields])
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The search was limited to papers published in English or where translations were available.

9.2 Appendix II - Glossary of terms

Algorithm – A process that is followed to allow a more efficient output.

Centripetal – A term used to describe movement towards the centre of an object.

Confrontational field testing – A gross qualitative examination technique that allows experienced clinicians to detect visual field defects.

Eccentricity – A term used to describe distance (in degrees) from the centre of the visual axis.

False negatives – A reliability index output calculated by presenting catch trials. A false negative occurs when a subject fails to detect a stimulus presented above the expected sensitivity threshold.

False positives – A reliability index output, presented as a proportion. False positives are produced when subjects respond without the presence of a stimulus.

Fixation losses – A reliability index output calculated from the proportion of positive responses given to presentations within the blind spot area i.e. an area where there is no sensitivity to light.

Fovea – A region at the back of the eye responsible for providing rich, detailed information from the centre of the visual field, i.e. what a person is looking at directly.

Goldmann nomenclature – Goldmann stimuli are characterised by a label three values in length. The first value is a Roman numeral from O to V. This numeral depicts the size of the Goldmann stimulus, with O being the smallest ($0.0625mm^2$) and V the largest ($64mm^2$). The next value is an Arabic numeral from 1 to 4, which represents the major intensity filter. One unit increase of this filter changes the intensity by 3.15 times, i.e. a 0.5 log unit change. The final value, a letter from 'a' to 'e', represents the minor

intensity filter. This filter produces a 0.1 log unit change in intensity. Thus, the largest, brightest Goldmann stimulus would be written: V4e.

Glaucoma – An eye disease, usually characterised by raised pressure within the eye (IOP) that leads to visual field loss.

Glaucoma Hemifield Test (GHT) – A summary statistic displayed at the end of a static perimetry test that compares 5 symmetrical regions above/below the horizontal midline to give an indicator of disease status by comparing the test outcome with expected (normative) values.

Isopter – A line drawn on a kinetic perimetry test result. The line represents a cut-off point, one side of the line representing an area of sensitivity, the other representing a lack of sensitivity. This line can be joined at either end to indicate an enclosed area of sensitivity.

Mean Deviation (MD) – A summary statistic displayed at the end of a static perimetry test, which is calculated by taking the mean of the 'total deviation' (TD) measures.

Meridian – In the context of kinetic perimetry it is used to define a straight line that extends from 0° eccentricity to the approximately 90° in length, travelling along a set angle (the angles are usually defined as starting at 0° and occurring every 15°).

Pattern Standard Deviation (PSD) – A summary statistic displayed at the end of a static perimetry test. PSD is a method of summarising deviation from 'normal' sensitivity, designed to highlight the presence of focal, rather than uniform field loss.

Perimeter – A device used to assess visual field function.

Perimetrist – A term used to describe the examiner conducting a perimetric test.

Perimetry – A term used to describe methods of assessing visual field function.

Retina – The surface at the back of the eye made of multiple layers, containing light-sensitive cells.

Scotoma (absolute) – An area of the visual field that does not demonstrate sensitivity to light.

Scotoma (relative) – An area of the visual field that demonstrates poor sensitivity to light.

Square root of loss variance (sLV) – An output produced by the Octopus perimeter to describe progressive visual field loss (see PSD).

Supra-threshold testing – A method of assessment that tests sensitivity to light. Commonly used for screening assessments.

Threshold testing – A method of assessment that tests a subject to the limit of their sensitivity.

Total Deviation (TD) – The absolute value difference between the measured sensitivity at a specific location, and the expected value at that location (derived from a normative database).

Visual Evoked Potentials (VEPs) – A measurement of electrical responses over the visual cortex taken when a subject is shown a visual stimulus. They require the placement of electrodes on a subjects head to record responses.

Visual Field Index (VFI) – A summary statistic displayed at the end of a static perimetry test. VFI aims to provide a summary (in percentage) of visual field sensitivity when compared to 'normal' function. It is formed from weighting pattern deviations, and places more weight on central visual field points.

9.3 Appendix III - Participant information sheets

9.3.1 Group A

Information for Children (5 – 8 years)

Study of Optimal Perimetric Testing In Children (OPTIC)

You are invited to take part in this research study

Why is the study being done?

We want to find out the best way to test visual fields in children.

This will help eye doctors treat children with eyesight problems.

What is a Visual Field Test?

A visual field test measures how far you can see up, down, and to the sides.

- The test does not hurt and is easy to do.
- You will not have any eye drops.

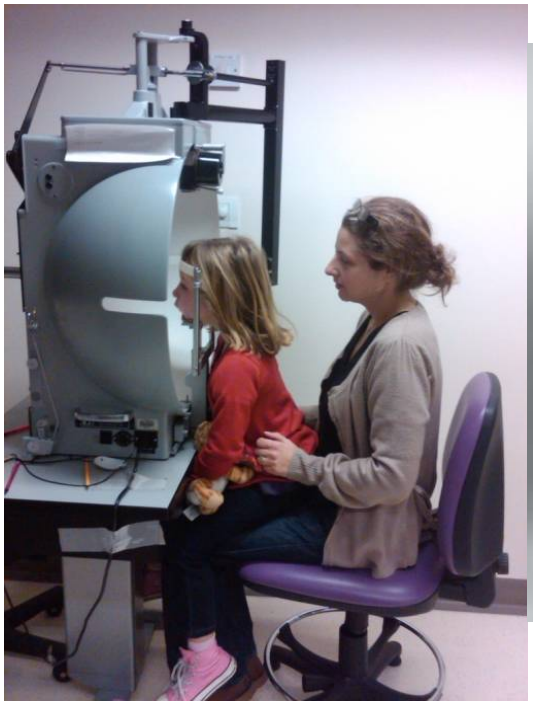
Where will I go for the tests?

You will come to the hospital clinic.

What will happen?

1. You will have three **visual field tests** using one eye only.
    - You will sit in front of a screen with your head resting on a chin pad so you can keep still (**like in the pictures**).
    - You will look at a point in the middle of the screen.
    - You will press a buzzer each time you see a small light on the screen.

Manual kinetic test



Automated static test

2. You will be asked what it was like to do the tests.

You may be asked to come back a few months later to visit the clinic to have the visual field tests done again.

Who will do the tests?

The eye doctor who explained this project to you.

How long will each visit take?

- Each visit will last up to 1 hour.
- During this time you will have rest breaks.

What happens to the results?

Your parent or guardian will be told the results of the test. We will keep the information safe and secure and will not tell anyone else the results.

Do I have to take part in this study?

No, you do not have to take part.

If you do take part, you can still stop at any time you want to.

Who do I contact if I want to know more?

You can contact any of the main researchers:

Mr Dipesh Patel
Research Assistant/Orthoptist
UCL Institute of Child Health
Tel: 079 3180 2207

OR

Professor Sir Peng Tee Khaw
Consultant Ophthalmologist
Principal Investigator at Moorfields Eye Hospital

OR

Chief Investigator:
Professor Jugnoo Rahi
Professor in Ophthalmic Epidemiology/Consultant Ophthalmologist

ADDRESS:
Centre for Paediatric Epidemiology and Biostatistics
Institute of Child Health,
30 Guilford Street,
London WC1N 1EH
Telephone: 020 7905 2835

Email: j.rahi@ucl.ac.uk
Email: dipesh_patel@ucl.ac.uk

If you decide to take part, your parent will let us know.

Thank you

Information for Children or Young People (9 – 15 years)
Study of Optimal Perimetric Testing In Children (OPTIC)

You are invited to take part in this research study

The aim of the study

We want to find out the best way to test visual fields in children and how children feel about having these tests. This will help eye doctors treat children with eyesight problems.

What is a Visual Field Test?

A visual field test measures how far you can see to the sides and up and down. It is painless, easy to do and you will not have any eye drops.

There are two ways of testing visual fields:

Kinetic test – You sit and look at a screen and identify a small target as it moves to different places on the screen.

Static test - You sit and look at a screen and identify a small target as it lights up in different places on the screen.

Why is the study being done?

We want to find out which of the two ways of testing is best for children of different ages and with different eye disorders. This project will compare the tests in children without visual field problems and those with eyesight problems.

Where will the study take place?

If you take part in the study you will come to the hospital clinic.

What will happen to me in the study?

When you come to the hospital -

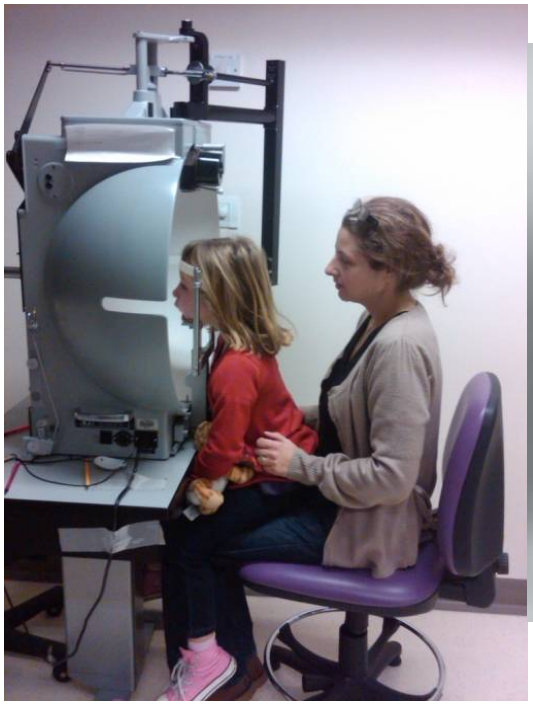
1. You will have both types of visual field test (two kinetic and one static). Only one eye will be tested.

   You will sit in front of a screen with your head resting on a chin pad so you can keep still (like in the pictures).

You will look at a point in the middle of the screen.

You will press a buzzer each time you see a light target somewhere on the screen.

Manual kinetic test



Automated static test

2. You will be asked a few questions about what it was like to do the visual field tests.

You may be asked to visit the clinic to have the visual field tests done again in a few months' time.

Who will carry out the tests?

The Research Orthoptist working on the study.

How long will each visit take?

Each visit will last 45 minutes to 1 hour in total – that is including all the tests and rest breaks.

What happens to the results?

Your parent or guardian will be told the results of the test. Then we will keep the information safe and secure and will not discuss your results with anyone who is not a part of our research team.

Do I have to take part in this study?

No, it is up to you. You are free to decide now or at any time during the research that you do not want to take part. You do not have to give a reason.

Who do I contact if I want to know more?

You can contact any of the main researchers:

Mr Dipesh Patel
Research Assistant/Orthoptist
UCL Institute of Child Health
Tel: 079 3180 2207

OR

Chief Investigator:

Professor Jugnoo Rahi

OR

Professor Sir Peng Tee Khaw
Consultant Ophthalmologist
Principal Investigator at Moorfields Eye Hospital

ADDRESS:
Centre for Paediatric Epidemiology and Biostatistics,
UCL Institute of Child Health,
30 Guilford Street, London
WC1N 1EH

Telephone: 020 7905 2835
Email j.rahi@ucl.ac.uk
Email: dipesh_patel@ucl.ac.uk

If you decide to take part, your parent will let us know.

Thank you

Information for Parents

Study of Optimal Perimetric Testing In Children (OPTIC)

We would like to ask your permission to include your child in this study

What is Perimetric Testing?

When you look at something you not only see the object you are looking at, but you can see the area around it. The total area that you can see (without moving your head or eyes) is called your **visual field**. Visual fields are measured using Perimetric Testing. These tests are used routinely by eye doctors. The results help in the diagnosis and monitoring of children with different types of eye conditions.

There are two main types of perimetric tests. Firstly, **kinetic perimetry** which involves looking at a screen and identifying a small light as it moves into different areas in your field of vision. This test is carried out manually by a tester, or by a machine. Secondly, **static perimetry** which involves looking at a screen and identifying a small target as it lights up in different areas in your field of vision. This test is automated. The tests are not uncomfortable and no eye drops are required.

During these tests your child would have to sit still, looking at a point in the centre of a screen, with his/her head resting on a chin-rest. The small lights are then displayed on the screen and your child has to press a hand-held buzzer each time they see a light.

Many perimetric tests are carried out each year in children, but it is still not known which is the best type of test to use for each eye condition.

The aim of the study

We want to do a 'head to head' comparison of static with kinetic perimetry, to find out the most effective way to test visual fields in children of different ages and with different types of eye conditions.

As a baseline for this, we need to know about the visual fields of children with good vision and no problems with their visual field.

What will the study involve?

If you and your child agree to take part we will arrange for you to visit the hospital for the study at a time that is convenient for you both.

At the first visit, your child will:

- have both static and kinetic visual field tests (only one eye will be tested)
- be asked a few questions about what it was like to do the tests

You may be asked to come back for a **second (final) visit, about 4 months later**, arranged at a time that is convenient for you and your child. The reason for repeating the tests is that we know there is some 'learning' involved, so that the results of the second test can be different (better) than the first. If you cannot come back we can still use the results from the first visit alone.

Each visit will last 45 minutes to 1 hour in total – that is including all the tests and rest breaks.

Your GP will be told if your child takes part in the study.

Will I know the results of the tests?

We will let you know the results of the test.

Your child is being asked to take part in the study because we expect him/her to have normal visual fields. However if the study tests are abnormal, we will arrange for you and your child to see the eye doctors to discuss the findings.

Who will have access to research records?

All information about your child will be treated in strict confidence by the researchers at all times. Only the researchers will have access to the actual data collected during this study and this data will be anonymised before it is analysed.

What are the potential benefits of taking part in this study?

This study will not benefit your child directly as he/she does not have visual field problems. However by taking part he/she will be making a valuable contribution to research which will help us improve how eye doctors diagnose and monitor children with various disorders that affect eyesight.

Does my child have to take part in this study?

It is up to you to decide. If you, or your child, decide now or at a later stage that you do **not** wish to take part in this project that is entirely your right. Whether or not your child takes part will in no way affect any present or future treatment he/she receives.

Will I be paid if my child takes part in this study?

You will not be paid for being in the study but, when you visit the clinic for a study visit, we will cover any travel and other necessary expenses.

Who do I speak to if problems arise?

If you have any questions or complaints about the way in which this research project has been, or is being conducted, please, in the first instance, discuss them with the researchers named below.

If the problems are not resolved, or you wish to comment in any other way, please contact the Head of Research and Development, by post via the Research and Development Office, Institute of Child Health, 30 Guilford Street, London WC1N 1EH, or if urgent, by telephone on 020 7242 9789.

Who do I contact if I want to know more?

You can contact any of the main researchers:

Mr Dipesh Patel
Research Assistant/Orthoptist
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OR

Professor Sir Peng Tee Khaw
Consultant Ophthalmologist
Principal Investigator at Moorfields Eye Hospital

OR

Chief Investigator:
Professor Jugnoo Rahi
Professor in Ophthalmic Epidemiology/Consultant Ophthalmologist

ADDRESS:
Centre for Paediatric Epidemiology and Biostatistics
Institute of Child Health,
30 Guilford Street,
London
WC1N 1EH

Telephone: 020 7905 2835
Email j.rahi@ucl.ac.uk
Email: dipesh_patel@ucl.ac.uk

9.3.2 Group B

Information for Children (5 – 8 years)

Study of Optimal Perimetric Testing In Children (OPTIC)

You are invited to take part in this research study

Why is the study being done?

We want to find out the best way to test visual fields in children.

This will help eye doctors treat children with eyesight problems.

What is a Visual Field Test?

A visual field test measures how far you can see up, down, and to the sides.

- The test does not hurt and is easy to do.
- You will not have any eye drops.

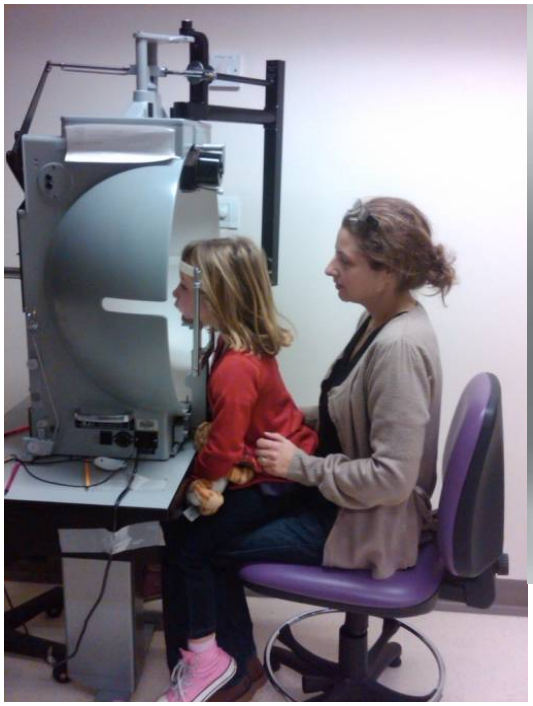
Where will I go for the tests?

You will come to the hospital clinic.

What will happen?

2. You will have two types of **visual field test** and each eye will be tested separately.
- You will sit in front of a screen with your head resting on a chin pad so you can keep still (**like in the picture**).
- You will look at a point in the middle of the screen.
- You will press a buzzer each time you see a small light on the screen.

Manual kinetic test **Automated static test**



2. You will be asked a few questions about what it was like to do the visual field tests.

You will be asked to visit the clinic to have the visual field tests done again in a few months.

Who will do the tests?

The eye doctor who explained this project to you.

How long will each visit take?

- Each visit will last up to 35 minutes.
- During this time you will have rest breaks.

What happens to the results?

Your parent or guardian will be told the results of the test. We will keep the information safe and secure and will not tell anyone else the results.

Do I have to take part in this study?

No, you do not have to take part.
If you do take part, you can still stop at any time you want to.

Who do I contact if I want to know more?

You can contact any of the main researchers:

Mr Dipesh Patel
Research Assistant/Orthoptist
UCL Institute of Child Health
Tel: 079 3180 2207

OR

Professor Sir Peng Tee Khaw
Consultant Ophthalmologist
Principal Investigator at Moorfields Eye Hospital

OR

Chief Investigator:
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WC1N 1EH

Telephone: 020 7905 2835
Email: j.rahi@ucl.ac.uk
Email: dipesh_patel@ucl.ac.uk

If you decide to take part, your parent will let us know.

Thank you

Information for Children or Young People (9 – 15 years)

Study of Optimal Perimetric Testing In Children (OPTIC)

You are invited to take part in this research study

The aim of the study

We want to find out the best way to test visual fields in children and how children feel about having these tests. This will help eye doctors treat children with eyesight problems.

What is a Visual Field Test?

A visual field test measures how far you can see to the sides and up and down. It is painless, easy to do and you will not have any eye drops.

There are two ways of testing visual fields:

Kinetic test – You sit and look at a screen and identify a small target as it moves to different places on the screen.

Static test - You sit and look at a screen and identify a small target as it lights up in different places on the screen.

Why is the study being done?

We want to find out which of the two ways of testing is best for children of different ages and with different eye disorders. This project will compare the tests in children with different types of eyesight problems.

Where will the study take place?

If you take part in the study you will come to the hospital clinic.

What will happen to me in the study?

When you come to the hospital -

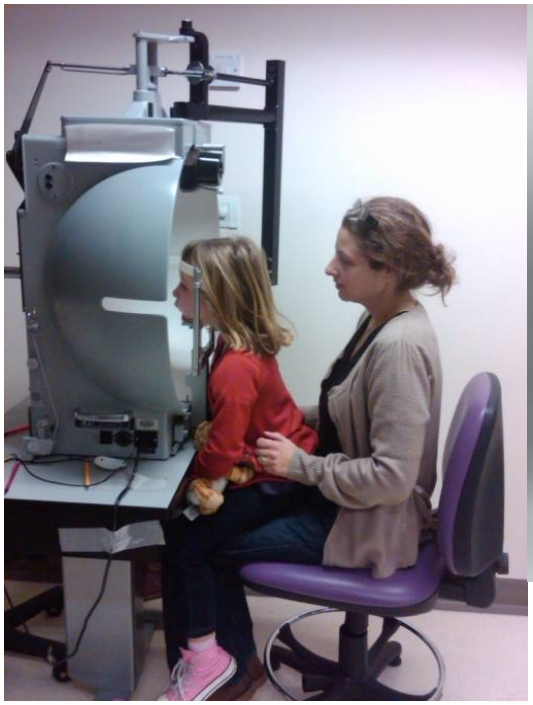
1. You will have both types of **visual field test (kinetic and static).** Each eye will be tested separately.

   You will sit in front of a screen with your head resting on a chin pad so you can keep still (like in the pictures).

   You will look at a point in the middle of the screen.

   You will press a buzzer each time you see a light target somewhere on the screen.

Manual kinetic test **Automated static test**



2. You will be asked a few questions about what it was like to do the visual field tests.

After a few months you will be asked to visit the clinic to have the visual field tests done again.

<u>Who will carry out the tests?</u>

The Research Orthoptist working on the study.

How long will each visit take?

Each visit will last up to 35 minutes in total – that is including all the tests and rest breaks.

What happens to the results?

Your eye doctor will be told the results of your test and will discuss it with your parent or guardian. Then we will keep the information safe and secure and will not discuss your results with anyone who is not a part of our research team.

Do I have to take part in this study?

No, it is up to you. You are free to decide now or at any time during the research that you do not want to take part. You do not have to give a reason.

Who do I contact if I want to know more?

You can contact any of the main researchers:

Mr Dipesh Patel
Research Assistant/Orthoptist
UCL Institute of Child Health
Tel: 079 3180 2207

OR

Prof Sir Peng Tee Khaw
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UCL Institute of Child Health, 30 Guilford Street, London, WC1N 1EH

Telephone: 020 7905 2835
Email: j.rahi@ucl.ac.uk
Email: dipesh_patel@ucl.ac.uk

If you decide to take part, your parent will let us know.

Thank you

Information for Parents

Study of Optimal Perimetric Testing In Children (OPTIC)

We would like to ask your permission to include your child in this study

What is Perimetric Testing?

When you look at something you not only see the object you are looking at, but you can see the area around it. The total area that you can see (without moving your head or eyes) is called your **visual field**. Visual fields are measured using Perimetric Testing. These tests are used routinely by eye doctors. The results help in the diagnosis and monitoring of children with different types of eye conditions.

There are two main types of perimetric tests. Firstly, **kinetic perimetry** which involves looking at a screen and identifying a small light as it moves into different areas in your field of vision. This test is carried out manually by a tester, or by a machine. Secondly, **static perimetry** which involves looking at a screen and identifying a small target as it lights up in different areas in your field of vision. This test is automated. The tests are not uncomfortable and no eye drops are required.

During these tests your child would have to sit still, looking at a point in the centre of a screen, with his/her head resting on a chin-rest. The small lights are then displayed on the screen and your child has to press a hand-held buzzer each time they see a light.

Many perimetric tests are carried out each year in children, but it is still not known which is the best type of test to use for each eye condition.

The aim of the study

We want to do a 'head to head' comparison of static with kinetic perimetry, to find out the most effective way to test visual fields in children of different ages and with different types of eye conditions.

What will the study involve?

If you and your child agree to take part we will arrange for you to visit the hospital for the study at a time that is convenient for you both.

At the first visit, your child will:

- have both static and kinetic visual field tests (each eye is tested separately)

- be asked a few questions about what it was like to do the tests

The first visit will last up to 35 minutes in total – that is including all the tests and rest breaks.

You may be asked to come back for a **second (final) visit, a few months later**, arranged at a time that is convenient for you and your child. The second visit is a short session testing two static visual field tests on one eye only. This takes approximately 10-15 minutes and will allow us to directly compare one short, and one slightly longer test.

After 12 months, we will gather more information from your child's medical notes to see how the visual field test results have contributed to the clinical care of your child.

Your GP will be told if your child takes part in the study.

Will I know the results of the tests?

We will let your child's eye doctor know the results of the tests immediately, as these are tests which your child would otherwise have had done as part of their normal care. Your eye doctor will discuss the findings of the perimetric testing with you.

Who will have access to research records?

All information about your child will be treated in strict confidence by the researchers at all times. Only the researchers will have access to the actual data collected during this study and this data will be anonymised before it is analysed.

What are the potential benefits of taking part in this study?

Your child would be having one of the visual field tests that we would plan to use in this study as a part of their current routine medical care. Our study is designed to find out, in a 'head to head' comparison, which type of test is best to use in diagnosing and monitoring children with particular conditions. We hope that in the future, understanding the most effective perimetric testing for each condition may benefit your child, and other children with similar eye conditions. By taking part in this study your child will be making a valuable contribution to this area of research.

Does my child have to take part in this study?

It is up to you to decide. If you, or your child, decide now or at a later stage that you do **not** wish to take part in this project that is entirely your right. Whether or not your child takes part will in no way affect any present or future treatment he/she receives.

Will I be paid if my child takes part in this study?

You will not be paid for being in the study, but if you choose to visit the clinic for a study visit outside of your normal hospital visits, we will cover any travel and other necessary expenses.

Who do I speak to if problems arise?

If you have any questions or complaints about the way in which this research project has been, or is being conducted, please, in the first instance, discuss them with the researchers named below.

If the problems are not resolved, or you wish to comment in any other way, please contact the Head of Research and Development, by post via the Research and Development Office, Institute of Child Health, 30 Guilford Street, London WC1N 1EH, or if urgent, by telephone on 020 7242 9789.

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Research Assistant/Orthoptist
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WC1N 1EH

Telephone: 020 7905 2835

Email j.rahi@ucl.ac.uk
Email: dipesh_patel@ucl.ac.uk

9.3.3 Group C

Information for Children (5 – 8 years)

Study of Optimal Perimetric Testing In Children (OPTIC)

You are invited to take part in this research study

Why is the study being done?

We want to find out the best way to test visual fields in children.

This will help eye doctors treat children with eyesight problems.

What is a Visual Field Test?

A visual field test measures how far you can see up, down, and to the sides.

- The test does not hurt and is easy to do.
- You will not have any eye drops.

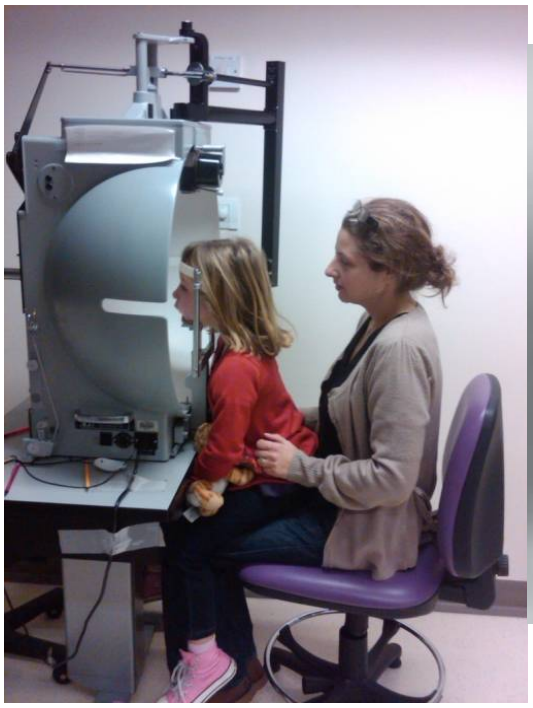
Where will I go for the tests?

You will come to the hospital clinic.

What will happen?

3. You will have a **visual field test.** Each eye will be tested separately.
    - You will sit in front of a screen with your head resting on a chin pad so you can keep still (**like in the pictures**).
    - You will look at a point in the middle of the screen.
    - You will press a buzzer each time you see a small light on the screen.

Manual kinetic test



Automated static test

2. You will be asked a few questions about what it was like to do the visual field tests.

A few months later you will be asked to visit the clinic to have the visual field tests done again.

Who will do the tests?

The eye doctor who explained this project to you.

How long will each visit take?

- Each visit will last up to 30 minutes.
- During this time you will have rest breaks.

What happens to the results?

Your parent or guardian will be told the results of the test. We will keep the information safe and secure and will not tell anyone else the results.

Do I have to take part in this study?

No, you do not have to take part.
If you do take part, you can still stop at any time you want to.

Who do I contact if I want to know more?

You can contact any of the main researchers:

Mr Dipesh Patel
Research Assistant/Orthoptist
UCL Institute of Child Health
Tel: 079 3180 2207

OR

Ms Bronwen Walters
Principal Investigator and
Head Orthoptist at Great Ormond Street Hospital

OR

Chief Investigator:
Prof Jugnoo Rahi
Professor in Ophthalmic Epidemiology

ADDRESS:

Life Course Epidemiology and Biostatistics Section
UCL Institute of Child Health
30 Guilford Street
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WC1N 1EH

Telephone: 020 7905 2835

Email: j.rahi@ucl.ac.uk
Email: dipesh_patel@ucl.ac.uk

<u>If you decide to take part, your parent will let us know.</u>

Thank you

Information for Children or Young People (9 - 15 years)

Study of Optimal Perimetric Testing In Children (OPTIC)

You are invited to take part in this research study

The aim of the study

We want to find out the best way to test visual fields in children and how children feel about having these tests. This will help eye doctors treat children with eyesight problems.

What is a Visual Field Test?

A visual field test measures how far you can see to the sides and up and down. It is painless, easy to do and you will not have any eye drops.

There are two ways of testing visual fields:

Kinetic test – You sit and look at a screen and identify a small target as it moves to different places on the screen.

Static test - You sit and look at a screen and identify a small target as it lights up in different places on the screen.

Why is the study being done?

We want to find out which of the two ways of testing is best for children of different ages and with different eye disorders. This project will compare the tests in children with different types of eyesight problems.

Where will the study take place?

If you take part in the study you will come to the hospital clinic.

What will happen to me in the study?

When you come to the clinic –

1. You will have a visual field test as part of your normal hospital visit.

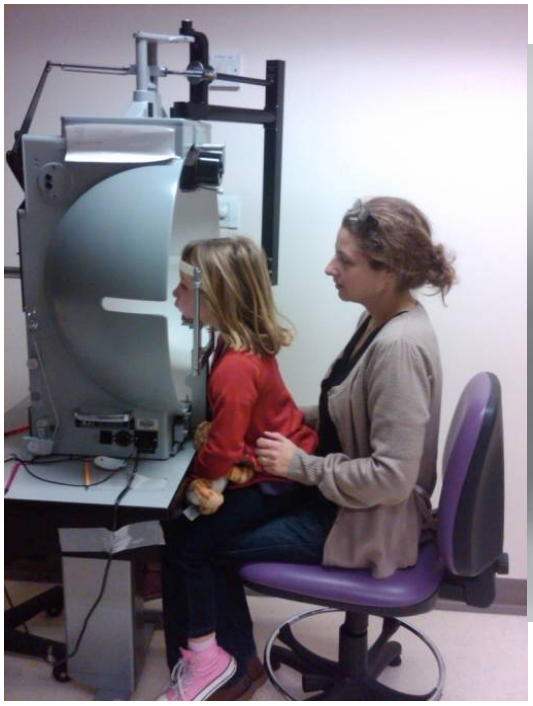
2. You will then have one extra visual field test**. Each eye will be tested** separately.

You will sit in front of a screen with your head resting on a chin pad so you can keep still (like in the pictures).

You will look at a point in the middle of the screen.

You will press a buzzer each time you see a light target somewhere on the screen.

Manual kinetic test



Automated static test

3. You will be asked a few questions about what it was like to do the visual field tests.

After about 4 months, you will be asked to visit the clinic to have the visual field tests done again.

After 12 months, information from your medical notes will be used to see how the visual field test results have been used by your eye doctors.

<u>Who will carry out the tests?</u>

The Research Orthoptist working on the study who is trained in testing eyesight and visual fields.

<u>How long will each visit take?</u>

Each visit will last around 30 minutes in total – that is including all the tests and rest breaks.

What happens to the results?

Your eye doctor will be told the results of your test and will discuss it with your parent or guardian. Then we will keep the information safe and secure and will not discuss your results with anyone who is not a part of our research team.

Do I have to take part in this study?

No, it is up to you. You are free to decide now or at any time during the research that you do not want to take part. You do not have to give a reason.

Who do I contact if I want to know more?

You can contact any of the main researchers:

Mr Dipesh Patel
Research Assistant/Orthoptist
UCL Institute of Child Health
Tel: 079 3180 2207

OR

Chief Investigator:
Prof Jugnoo Rahi
Professor in Ophthalmic Epidemiolog

OR

Ms Bronwen Walters
Principal Investigator and
Head Orthoptist at Great Ormond Street Hospital

ADDRESS:
Life Course Epidemiology and Biostatistics Section
UCL Institute of Child Health, 30 Guilford Street,
London, WC1N 1EH
Telephone: 020 7905 2835
Email: j.rahi@ucl.ac.uk
Email: dipesh_patel@ucl.ac.uk

If you decide to take part, your parent will let us know.
Thank you

Information for Parents

Study of Optimal Perimetric Testing In Children (OPTIC)

We would like to ask your permission to include your child in this study

What is Perimetric Testing?

When you look at something you not only see the object you are looking at, but you can see the area around it. The total area that you can see (without moving your head or eyes) is called your **visual field**. Visual fields are measured using Perimetric Testing. These tests are used routinely by eye doctors. The results help in the diagnosis and monitoring of children with different types of conditions.

There are two main types of perimetric tests. Firstly, **kinetic perimetry** which involves looking at a screen and identifying a small light target as it moves into different areas in your field of vision. This test is carried out manually by a tester or can be automated. Secondly, **static perimetry** which involves looking at a screen and identifying a small target as it lights up in different areas in your field of vision. This test is automated. The tests are not uncomfortable and no eye drops are required.

During these tests your child would have to sit still, looking at a point in the centre of a screen, with his/her head resting on a chin-rest. The small lights are then displayed on the screen and the child has to press a hand-held buzzer each time they see a light.

Many perimetric tests are carried out each year in children, but it is still not known which is the best type of test to use for each eye condition.

The aim of the study

We want to do a 'head to head' comparison of static with kinetic perimetry testing, to find out the most effective way to test visual fields in children of different ages and with different types of eye conditions. We also want to compare a new test with the standard test in use today.

What will the study involve?

If you and your child agree to take part we will arrange for you to visit the hospital for the study at a time that is convenient for you both.

At the visit, your child will:

- have an automated kinetic visual field test OR an automated static visual field test (each eye is tested separately)

- be asked a few questions about what it was like to do the test

We will look at your child's medical notes to collect information about the kinetic visual field tests that your child has had previously.

You will be invited back for a **second (final) visit, about 4 months later,** arranged at a time that is convenient for you and your child. The reason for returning is so that we can compare your child's responses to a different test on the next visit. You can still participate in this study with only one visit.

Each visit will last approximately 30 minutes in total – that is including all the tests and rest breaks.

After 12 months, we will gather more information from your child's medical notes to see how the visual field test results have contributed to the clinical care of your child.

Your GP will be told if your child takes part in the study.

Will I know the results of the tests?

We will let your child's eye doctor know the results of the tests immediately, as these are tests which your child would otherwise have had done as part of their normal care. Your eye doctor will discuss the findings of the perimetric testing with you.

Who will have access to research records?
All information about your child will be treated in strict confidence by the researchers at all times. Only the researchers will have access to the actual data collected during this study and this data will be anonymised before it is analysed.

What are the potential benefits?
Your child has already had kinetic perimetric tests. Our study is designed to find out, in a 'head to head' comparison, which type of test is best to use in diagnosing and monitoring children with particular conditions. We hope that in the future, understanding the most effective perimetric testing for particular conditions may benefit your child, and other children with similar eye conditions. By taking part in this study your child will be making a valuable contribution to this area of research.

Does my child have to take part in this study?
It is up to you to decide. If you, or your child, decide now or at a later stage that you do **not** wish to take part in this research project that is entirely your right. Whether or not your child takes part will in no way affect any present or future treatment he/she receives.

Will I be paid if my child takes part in this study?
You will not be paid for being in the study but, when you visit the clinic for a study visit, we will cover any travel and other necessary expenses.

Who do I speak to if problems arise?
If you have any questions or complaints about the way in which this research project has been, or is being conducted, please, in the first instance, discuss them with the researchers named below.

If the problems are not resolved, or you wish to comment in any other way, please contact the Head of Research and Development, by post via the Research and Development Office, Institute of Child Health, 30 Guilford Street, London WC1N 1EH, or if urgent, by telephone on 020 7242 9789.

Who do I contact if I want to know more?

You can contact any of the main researchers:

Mr Dipesh Patel
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Telephone: 020 7905 2835

Email: j.rahi@ucl.ac.uk
Email: dipesh_patel@ucl.ac.uk

9.4 Appendix IV - Parental consent form

Moorfields Study ID: KHAP1026

Subject Identification No for this study: _____

Parent/Guardian CONSENT FORM

Project Title: Study of Optimal Perimetric Testing In Children (OPTIC)

Investigators: Professor Sir Peng Khaw, Professor Jugnoo Rahi

Please **initial box** to indicate agreement:

1	I confirm that I have read and understand the information sheet dated 04/05/2012 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2	I understand that my child's participation is voluntary and that he/she is free to withdraw at any time, without giving any reason, without his/her medical care or legal rights being affected.	
3	I understand that relevant sections of any of my child's medical notes and data collected during the study may be looked at, by employees from regulatory authorities or from the Research and Development Offices of Great Ormond Street Hospital or the UCL Institute of Child Health, where it is relevant to my child's taking part in this research. I give permission for these individuals to have access to my child's records.	
4	I understand that all data collected during the study will be anonymised and then analysed by the research team based at the Institute of Child Health. I give permission for these individuals to use my child's anonymised study data.	
5	I agree to my child's GP being informed of his/her participation in the study.	
6	I agree to my child taking part in the above study.*	

* If you as the parent/guardian lose the capacity to consent to your child's participation, your child will not continue any further in the study but anonymised data collected about your child up to that point will be used in the analysis.

_____

Name of Child

_____	_____	_____
Name of Parent/Guardian	Date	Signature
_____	_____	_____
Name of Person taking consent (if different from Investigator)	Date	Signature
_____	_____	_____
Investigator	Date	Signature

9.5 Appendix V – Sample of test order randomisation

1 = Goldmann
2 = Octopus
3 = Humphrey

1 = Right Eye
2 = Left Eye

Study ID	**Eye Order**			**Test Order**				
2001	1	2	1	3	1	1	1	1
2002	2	2	2	2	3	2	2	1
2003	1	1	3	2	1	2	3	1
2004	1	3	2	2	3	1	3	2
2005	1	1	3	1	1	1	3	1
2006	1	1	1	3	2	2	2	2
2007	2	3	2	1	3	2	3	3
2008	1	3	1	2	3	1	2	2
2009	2	3	1	3	3	1	2	1
2010	2	3	1	3	2	1	3	1
2011	2	1	2	3	2	2	1	3
2012	2	2	1	3	2	2	1	3
2013	1	1	1	3	3	1	2	1
2014	1	3	2	1	2	2	3	2
2015	2	2	2	2	1	3	1	1
2016	2	2	1	2	2	1	2	2
2017	2	3	3	1	3	3	2	1
2018	1	3	2	2	1	1	3	1
2019	2	3	2	2	1	1	3	2

9.6 Appendix VI – `kineticF` code

The following section lists one working example of the R code developed for this study (developed by DEP and MCB). The code developed (section 9.6.2 (pg. 228)) was adapted to meet CRAN policies and published as the R library package `'kineticF'` available from:

https://cran.r-project.org/web/packages/kineticF/index.html

9.6.1 `set.template()` - Kinetic perimetry grid plot

Code was developed to digitally visualise kinetic perimetry results. A custom grid plot was created to allow interpretation of results for clinicians used to viewing Goldmann plots. As such, it was not appropriate to simply create a circular plot of radius 90°. The following code is presented in the order that it appears in the function. The programme (R) layers images on top of the previous command, so text must be added last to keep it at the forefront of the image.

Firstly, the grid dimensions were set to rough dimensions:

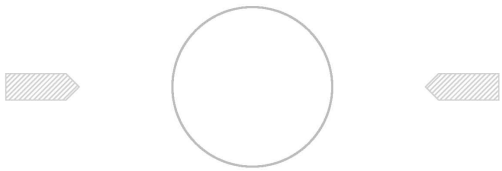
```
> eqscplot(c(-90,90), c(-70,70), ylim=c(-70, 70), axes=F,
type="n",xlab="",ylab="")
```

Then, the two 'void' sections in the Goldmann bowl were delineated and filled with grey lines:

```
> rad.aux<- 92.5

> polygon(c(-rad.aux, -70, -65, -70, -rad.aux),c( 5,5,0,-5,-5),
density=25, col='lightgray')

> polygon(c(rad.aux, 70, 65, 70, rad.aux),c( 5,5,0,-5,-5),
density=25, col='lightgray')
```

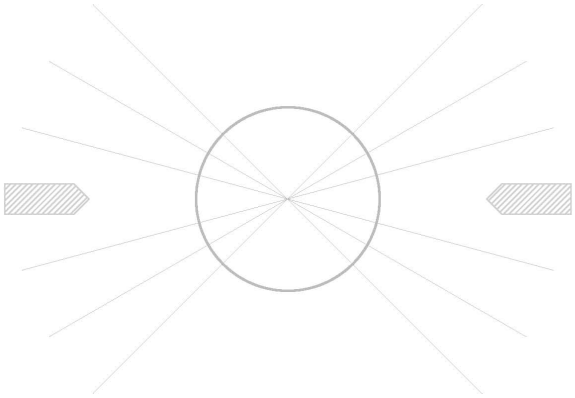
Following this, a thick circle was plotted with a radius of 30°, centred in the middle of the plot:

```
> draw.circle( 0,0, radius=30,border='gray', lwd=2 ,nv=500)
```



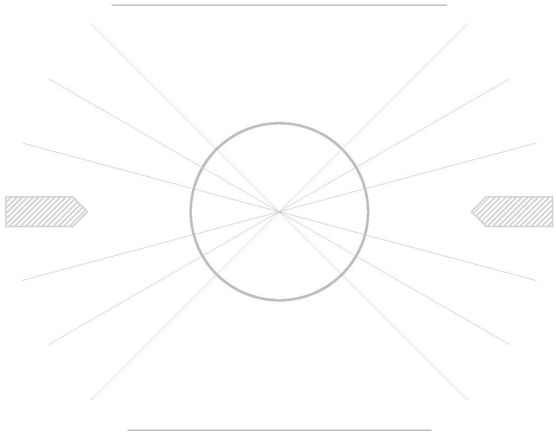
Then, lines were calculated and plotted, from the centre along 12 meridia, separated by 15°, of length 90°:

```
> seq.angles<- seq(0, 180, by=15)
> ind.angles1<- c(1:3, 9:11 )### complete lines
> for ( i in ind.angles1)
  {
        segments(0,0, 90*cos(2*pi*i/24), 90*sin(2*pi*i/24),
                  lwd=1/2, col='gray')
        segments(0,0, -90*cos(2*pi*i/24), -90*sin(2*pi*i/24),
                  lwd=1/2, col='gray')
  }
```



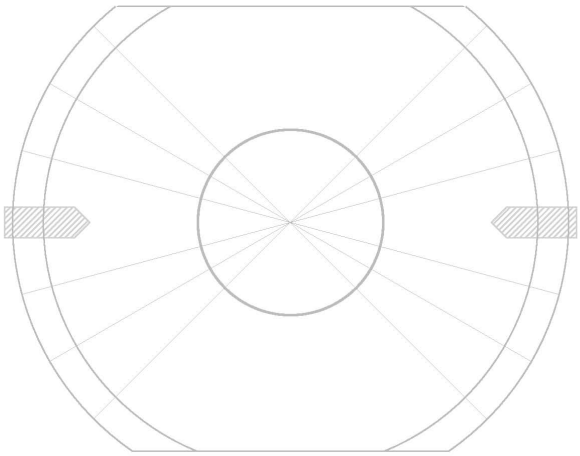
Then, the vertical limits of the grid were defined. This was set at y=70 and y=-74 to emulate Goldmann plots:

```
> upper.corner<- sqrt(c(80,90)^2 - 70^2)

> segments(-upper.corner, 70, upper.corner, 70,col='gray',
lwd=1)


> lower.corner<- sqrt( c(80,90)^2 - 74^2)

> segments(-lower.corner, -74, lower.corner, -74,col='gray',
lwd=1)
```



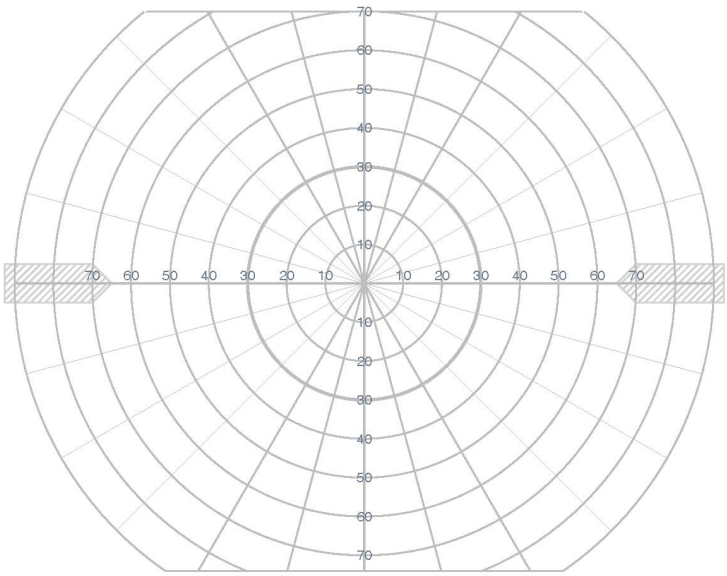
Arcs were then created to join the two vertical lines, one of radius ±80° and one of ±90°:

```
> draw.arc(0,0, 90, angle1=asin(70/90), angle2=asin(-74/90),
           col='gray',lwd=1)
> draw.arc(0,0, 80, angle1=asin(70/80), angle2=asin(-74/80),
           col='gray',lwd=1)

> draw.arc(0,0, 90, deg1= 180+asin(-70/90)*180/pi,
           deg2= 180+asin(74/90)*180/pi,
           col='gray',lwd=1)

> draw.arc(0,0, 80, deg1= 180+asin(-70/80)*180/pi,
           deg2= 180+asin(74/80)*180/pi,
           col='gray',lwd=1)

> draw.arc(0,0,90, deg1=180+asin(-70/90)*180/pi,
           deg2=asin(70/90)*180/pi, col='white',
           lwd=1)
```



The x and y axis line were then plotted along with the missing segment lines. Circles every 10° up to 70° were also plotted and labelled:

```
> segments(0, -74, 0, 70, col='gray')
> segments(-90, 0, 90, 0, col='gray')

> segments(rep(0,4), rep(0,4),
           70/tan(rad(c(60,75,105,120))), rep(70,4),
           col='gray', lwd=1)

> segments(rep(0,4), rep(0,4),
           -74/tan(rad(c(240,255,285,300))), rep(-74,4),
           col='gray', lwd=1)

> for ( i in seq(10,70,by=10))
  {
     draw.circle( 0,0, radius=i,border='gray', nv=500)
     text( 0, -i,  i, cex=2/3, col='slategray')
     text( 0, i, i, cex=2/3, col='slategray')
     text( -i,2, i, cex=2/3, col='slategray')
     text(i,2,i,cex=2/3, col='slategray')
  }
```

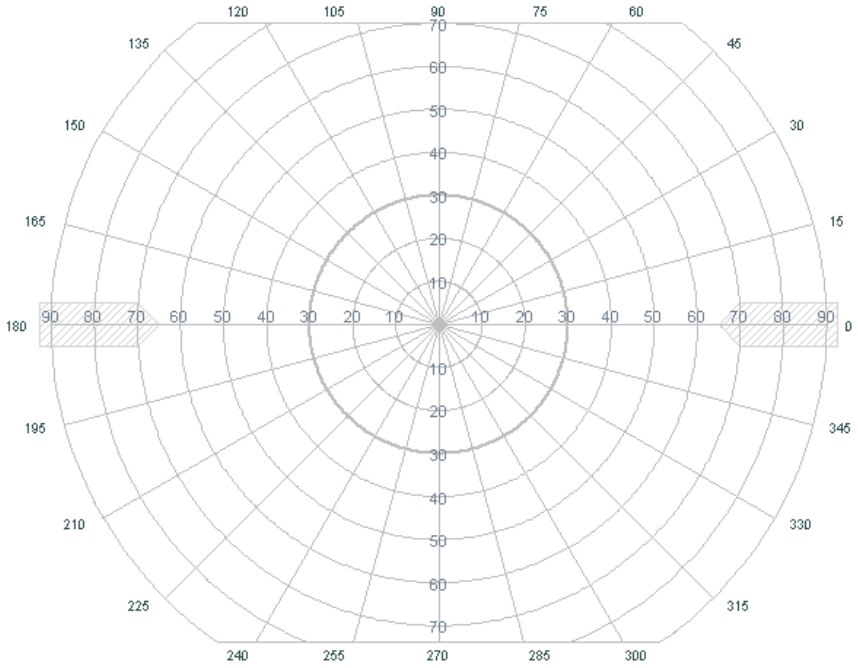


NOTE: These lines were all of uniform weight, with the 30° radius line being the only thicker line.

Finally, text was inserted for the 80° and 90° radius circles. Then, the axes were labelled around the outside of the plot and offset a small distance to improve legibility, completing the grid:

```
> text(c(-80,-90,80,90),rep(2,4), rep(c(80,90),2),
       cex=2/3, col='slategray')


> text(par()$usr[1] -4, 0, "180",
       col='darkslategray',cex=3/5,family='sans')
> text(par()$usr[2] + 2, 0, "0",
       col='darkslategray',cex=3/5, family='sans')


> for (i in seq.angles[-c(1, 5:13, length(seq.angles))])
        text(  rad.aux*cos(rad(i)), rad.aux*sin(rad(i)), i,
        col='darkslategray',cex=3/5, family='sans',pos=4,
```

```
        offset=1/4)

> for (i in seq.angles[5:9])
       text(  rad.aux*cos(rad(i)), rep(70,5), i,
       col='darkslategray',cex=3/5, family='sans',pos=3,
       offset=1/4)

> for (i in seq.angles[-c(1, 2:9, length(seq.angles))])
       text(  rad.aux*cos(rad(i)), rad.aux*sin(rad(i)), i,
       col='darkslategray',cex=3/5, family='sans',pos=2,
       offset=1/4)

> for (i in 180+seq.angles[-c(1,5:13,length(seq.angles))])
       text( rad.aux*cos(rad(i)), rad.aux*sin(rad(i)), i,
       col='darkslategray',cex=3/5, family='sans', pos=2,
       offset=1/4)

> for (i in 180+seq.angles[5:9])
       text(  rad.aux*cos(rad(i)), -rep(74,5), i,
       col='darkslategray',cex=3/5, family='sans',pos=1,
       offset=1/4)

> for (i in 180+seq.angles[-c(1, 2:9, length(seq.angles))])
       text(  rad.aux*cos(rad(i)), rad.aux*sin(rad(i)), i,
       col='darkslategray',cex=3/5, family='sans',pos=4,
       offset=1/4)
```



This code was compiled into a function `set.template()` and can be run at any time to create a blank visual field plot.

9.6.2 `kineticF` code

A full list of the code developed for `kineticF` is listed here, starting with data cleaning and organisation, followed by functions for analysis.

```
### Delete unwanted isopter points

delete.points<- function(outer.iso)

{

### this programme deletes practice and error points selected
using locator()

### outer.iso is a matrix containing practice and error points

### output is a matrix excluding the identified points called
outer.iso too



set.template()
```

```
title(main='Delete unwanted isopter points')

points(outer.iso[,1], outer.iso[,2], pch=19, col='black')

n.pts<- dim( outer.iso)[1]

s1<- 1:(n.pts-1)


deleted.index<- identify( outer.iso[,1], outer.iso[,2],
pos=TRUE)$ind

### extracts indices of manually selected points

if(length(deleted.index >0)) outer.iso<- outer.iso[-
deleted.index, ]

dimnames( outer.iso)[[1]]<- 1:dim( outer.iso)[1]


invisible(outer.iso)

} ### end of delete.points




### Re-order isopter matrix

stop.identify<- function( xy)

{

#### xy is an n x 2 matrix with positions of points

#### ordered.list is a vector containing an ordered list of
identified points


set.template()

title(main='Join isopter points in order starting at 180
degrees working clockwise')


points( xy, pch=19)

ordered.list<-NA
```

```
stop1<- FALSE
for (i in 1:1000)
{
  while(!stop1)
    {
      aux<- identify( xy, n=1)
      stop1<- length( aux)==0
      ordered.list<- c( ordered.list, aux)
     }
}
ordered.list[-1]
} ### end of stop.identify



### Distance function for reliability measure
dist2full <- function(dis)
{
#### dis is a vector of distances between n points
### returns a symmetric matrix of size n x n
     n <- attr(dis, "Size")
     full <- matrix(0, n, n)
     full[lower.tri(full)] <- dis
     full + t(full)
} ### end of dist2full



set.template<- function(void=TRUE)
{
```

```
setWindowTitle(getwd())


#### generates visual field template

#### void == TRUE produces a hashed area at 0 deg and 180 deg


require(MASS)

require(plotrix)

require(splancs)

require(circular)


par(pty='m')

par(xpd=TRUE)


eqscplot(c(-90,90), c(-70,70), ylim=c(-70, 70), axes=F,

type="n",xlab="",ylab="")

rad.aux<- 92.5


if(void)

{

polygon(c(-rad.aux, -70, -65, -70, -rad.aux),c( 5,5,0,-5,-5),
density=25, col='lightgray')

polygon(c(rad.aux, 70, 65, 70, rad.aux),c( 5,5,0,-5,-5),
density=25, col='lightgray')

}


draw.circle( 0,0, radius=30,border='gray', lwd=2 ,nv=500)

seq.angles<- seq(0, 180, by=15)

ind.angles1<- c(1:3, 9:11 )### complete lines

for ( i in ind.angles1)
```

```
{
segments(0,0, 90*cos(2*pi*i/24), 90*sin(2*pi*i/24),
         lwd=1/2, col='gray')
segments(0,0, -90*cos(2*pi*i/24), -90*sin(2*pi*i/24),
         lwd=1/2, col='gray')
}

### obtain corners
upper.corner<- sqrt(c(80,90)^2 - 70^2)
segments(-upper.corner, 70, upper.corner, 70,col='gray', lwd=1)

lower.corner<- sqrt( c(80,90)^2 - 74^2)
segments(-lower.corner, -74, lower.corner, -74,col='gray',
lwd=1)

draw.arc(0,0, 90, angle1=asin(70/90), angle2=asin(-74/90),
col='gray',lwd=1)
draw.arc(0,0, 80, angle1=asin(70/80), angle2=asin(-74/80),
col='gray',lwd=1)

draw.arc(0,0, 90, deg1= 180+asin(-70/90)*180/pi,
         deg2= 180+asin(74/90)*180/pi,
         col='gray',lwd=1)

draw.arc(0,0, 80, deg1= 180+asin(-70/80)*180/pi,
         deg2= 180+asin(74/80)*180/pi,
         col='gray',lwd=1)

### remove upper and lower caps
```

```
draw.arc(0,0,90, deg1=180+asin(-70/90)*180/pi,
         deg2=asin(70/90)*180/pi, col='white',
         lwd=1)
### draw major axes

segments(0, -74, 0, 70, col='gray')
segments(-90, 0, 90, 0, col='gray')

segments(rep(0,4), rep(0,4),
         70/tan(rad(c(60,75,105,120))), rep(70,4),
         col='gray', lwd=1)

segments(rep(0,4), rep(0,4),
         -74/tan(rad(c(240,255,285,300))), rep(-74,4),
         col='gray', lwd=1)

for ( i in seq(10,70,by=10))
{
draw.circle( 0,0, radius=i,border='gray', nv=500)
text( 0, -i,  i, cex=2/3, col='slategray')
text( 0, i, i, cex=2/3, col='slategray')
text( -i,2, i, cex=2/3, col='slategray')
text(i,2,i,cex=2/3, col='slategray')
}

text(c(-80,-90,80,90),rep(2,4), rep(c(80,90),2),
cex=2/3, col='slategray')
```

```
text(par()$usr[1] -4, 0, "180", col='darkslategray',cex=3/5,
family='sans')

text(par()$usr[2] + 2, 0, "0", col='darkslategray',cex=3/5,
family='sans')


for (i in seq.angles[-c(1, 5:13, length(seq.angles))])

   text(  rad.aux*cos(rad(i)), rad.aux*sin(rad(i)), i,

   col='darkslategray',cex=3/5, family='sans',pos=4,

   offset=1/4)


for (i in seq.angles[5:9])

   text(  rad.aux*cos(rad(i)), rep(70,5), i,

   col='darkslategray',cex=3/5, family='sans',pos=3,

   offset=1/4)


for (i in seq.angles[-c(1, 2:9, length(seq.angles))])

   text(  rad.aux*cos(rad(i)), rad.aux*sin(rad(i)), i,

   col='darkslategray',cex=3/5, family='sans',pos=2,

   offset=1/4)


for (i in 180+seq.angles[-c(1,5:13,length(seq.angles))])

   text( rad.aux*cos(rad(i)), rad.aux*sin(rad(i)), i,

   col='darkslategray',cex=3/5, family='sans', pos=2,

   offset=1/4)


for (i in 180+seq.angles[5:9])

   text(  rad.aux*cos(rad(i)), -rep(74,5), i,

   col='darkslategray',cex=3/5, family='sans',pos=1,
```

```
   offset=1/4)


 for (i in 180+seq.angles[-c(1, 2:9, length(seq.angles))])
   text(  rad.aux*cos(rad(i)), rad.aux*sin(rad(i)), i,
   col='darkslategray',cex=3/5, family='sans',pos=4,
   offset=1/4)


}



check.directory.exists<- function(mainDir=getwd(), subDir)
{
### mainDir is normally the current working directory
### subDir is a string with the name of the subdirectory where
### files are stored
### if path subDir doesn't exist then create


if(!file.exists(subDir))
    {
         dir.create(file.path(mainDir, subDir))
         print(paste('directory ', subDir,' created on ',
date()),quote=FALSE)
    }
else print(paste('directory ', subDir, ' already
exists'),quote=FALSE)


invisible(NULL)
}
```

```
preprocess.octopus<- function(octopus.file,
                    input.directory='Octopus\\Octopus_raw',
                    output.directory='Octopus\\Octopus_data',
              demogr.file='Octopus\\Octopus_demographics.csv')
{
## This function is used to clean Octopus data - one subject at
a time
### input.directory is the name of the directory where the
input raw data are contained
### output.directory is the name of the directory where the
output of
### preprocessing is stored
### demogr.file is the name of the demographic file with
columns
### ID, Eye tested, Sex, age, test quality
###
### output is matrix Mfile containing coordinates and isopter
labels
### for the subject
### Note that this function writes a subject-specific set of
*.csv files
### one per isopter
### If there is 1 or 0 points it crashes!

check.directory.exists(subDir=output.directory)
demogr<- read.csv(demogr.file, header=TRUE)

Mfile<- scan(file=paste(input.directory,octopus.file,sep='\\'),
what='', sep=';')
### test for apostrophes in all positions
```

```
if( length(Mfile) < 5)

{

warning("please check for and remove apostrophes in subject's
name")

return(invisible(NULL))

}


### get the 1st field and assign it as the name of the
data.frame


id<- Mfile[1] ### subject id


eye.side<- substring(as.character(demogr[ match(id,
demogr[,1]), 2]),1,1)


Mfile<- Mfile[-(1:32)] ### exclude identifiers ###

### 32 characters is standard length for identifiers

Mfile<- Mfile[-length(Mfile)]


Mfile<- as.numeric(Mfile)


pos.outliers<- (1:length(Mfile))[ abs(Mfile) > 100]

num.outliers<- length(pos.outliers)

outliers<-Mfile[pos.outliers]


if(length(pos.outliers)>0)

  {

   Mfile<- Mfile[-pos.outliers] ### Values can't be > 100
degrees
```

```
   print(paste(num.outliers,' outliers removed', outliers,
collapse='',

   sep=' : '),quote=FALSE)

  }


Mfile<- matrix( Mfile, ncol=11, byrow=TRUE)


### variable description

###  1 - 2       start points

###  3 - 4       direction - NB (0,0) for centripetal
presentation

###  5 - 6       responses to be plotted

###  7 - 8       undefined (0's)

###  9           intensity (decibels)

###  10          size (mm^2)

###  11          speed (deg/sec)


Mfile<- as.data.frame(Mfile)

names(Mfile)<- c('start1','start2','direction1','direction2',

                 'X', 'Y', 'null1','null2',

                 'intensity','size','speed')


### define labels for isopters

labels<- c('III4e', 'I4e', 'I2e', 'blind')

### patterns: 00015 = I4e;   00035 = III4e; 001015 = I2e

### anything ending in "2" is blind


### chop Mfile into isopters

n.rows<- dim( Mfile)[1]
```

```
patterns.isopters<- apply(Mfile[,7:11],1, function( x){
paste(x, collapse='')} )

num.isopters<- length( unique( patterns.isopters))

s1<- 2:n.rows

pos.changes<- (1:n.rows)[ patterns.isopters[s1-1] !=
patterns.isopters[s1]]

pos.changes<- c(0, pos.changes, n.rows)


labels.isopters<- ifelse(patterns.isopters=='00015', 'I4e',

                 ifelse(patterns.isopters=='00035', 'III4e',

                 ifelse(patterns.isopters=='001015', 'I2e',
'blind')))


Mfile$labels.isopters<- labels.isopters


### the output of preprocess.octopus must be num.isopters .csv
files

for( i in 1:num.isopters)

{

file.name<- paste(output.directory, paste(id, eye.side, 'O',


Mfile$labels.isopters[pos.changes[i]+1],'.csv',sep=''),
sep='\\')


print(file.name)

s1<- (pos.changes[i]+1) : (pos.changes[i+1])

write.csv(file=file.name, x=Mfile[s1, 5:6], row.names=FALSE)

} ### close loop over number of isopters




### returns the whole data.frame for inspection
```

```
### but only if preprocess.octopus is assigned to an object

invisible( Mfile[,c('X','Y', 'labels.isopters')])

}


### output of preprocess.octopus is num.isopters *.csv files
in format X,Y

### NB these files have to be cleaned using plot.individual




plot.individual<-

function(file.name, dir.name='Goldmann\\Goldmann_data',
perimeter='G',

         deactivate.cleaning=TRUE,

         skip.reliability.meas=FALSE, no.flip=TRUE)

{

### file.name is the file name using format defined for studyid

### note that argument file.name only contains e.g. "M2005R"

### dir.name is the data directory name - assume it's below
getwd()

### perimeter must be either "G" (Goldmann) or "O" (Octopus)

### if deactivate.cleaning==TRUE it assumes a pre-ordered
dataset (Goldmann)

### if deactivate.cleaning==FALSE it assumes no ordered
(Octopus data)

###    and starts cleaning procedure

### if skip.reliability.meas==FALSE then there's no kinetic
perimetry

###    reliability measure (KPRM)

### if no.flip==TRUE then display it as the original left/right
eye

### if no.flip==FALSE then flip and display as right eye
```

```
### Assumes that Octopus\\Octopus_data exists


if(!deactivate.cleaning) print("You're now starting data
cleaning")


if(perimeter!='G')

{

set.template(void=FALSE)

}

else

set.template()


dists<- areas<- rep(NA, 4)


if(perimeter!= 'O' & perimeter!= 'G') stop('perimeter value is
invalid')


file0<- paste(dir.name, file.name,sep='\\')

file1<- paste(file0, perimeter, 'III4e.csv', sep='')

file2<- paste(file0, perimeter, 'I4e.csv', sep='')

file3<- paste(file0, perimeter, 'I2e.csv', sep='')

file4<- paste(file0, perimeter, 'blind.csv', sep='')

file5<- paste(file0, perimeter,'rmeas.csv', sep='')


which.files <-file.exists(c(file1, file2, file3, file4, file5))


III4e<-I4e<-I2e<-blind<-rmeas<-NULL ### initialise


if(which.files[1])
```

```
{
   aux1<- read.csv(file1, header=TRUE)
   III4e <- rbind(aux1, aux1[1,])
   III4e <- cbind(III4e[,1], III4e[,2])
}

if(which.files[2])
{
   aux1<- read.csv(file2, header=TRUE)
   I4e <- rbind(aux1, aux1[1,])
   I4e <- cbind(I4e[,1], I4e[,2])
}

if(which.files[3])
{
   aux1<- read.csv(file3, header=TRUE)
   I2e <- rbind(aux1, aux1[1,])
   I2e <- cbind(I2e[,1], I2e[,2])
}

if(which.files[4])
{
   aux1<- read.csv(file4, header=TRUE)
   blind <- rbind(aux1, aux1[1,])
   blind <- cbind(blind[,1], blind[,2])
}

if(which.files[5]) rmeas<- read.csv(file5, header=TRUE)
```

```
side.eye<- substring(file.name, 6,6) ## must be L or R only



if(deactivate.cleaning) ### starts Goldmann
{



if(side.eye=='L' & !no.flip)
{
   if( which.files[1]) III4e[,1]<- -III4e[,1]
   if( which.files[2]) I4e[,1]<- -I4e[,1]
   if( which.files[3]) I2e[,1]<- -I2e[,1]
   if( which.files[4]) blind[,1]<- -blind[,1]
  if( which.files[5]) rmeas[,1] <- -rmeas[,1]
}



   if(which.files[1])
   {
   ##III4e
   points(III4e, pch=4, col='black', lwd=2, cex=2/3)
   if(deactivate.cleaning) lines(III4e, col= "black", lwd=2)
   areas[1]<- areapl(III4e)
   }

   if(which.files[2])
{
```

```
##I4e
points(I4e, pch=19, col='royalblue3')
if(deactivate.cleaning) lines(I4e, col= "royalblue3", lwd=2)
areas[2]<- areapl(I4e)
}

if(which.files[3])
{
##I2e
points(I2e, pch=15, col='maroon', lwd=2, cex=2/3)
if(deactivate.cleaning) lines(I2e, col="maroon", lwd=2)
areas[3]<- areapl(I2e)
}

if(which.files[4])
{
##Blind spot
points(blind, pch=4, col='maroon', lwd=2, cex=1/3)
if(deactivate.cleaning) lines(blind, col="maroon", lwd=2)
areas[4]<- areapl(blind)
}

if(which.files[5] & !skip.reliability.meas)
{
## Reliability measure points
points(rmeas, pch=2, cex=2/3, col="red", lwd=2)
print(
cat('please identify four points on the plot','\n',
```

```
   'starting in the upper-left quadrant working
clockwise','\n'),

quote=FALSE)


if(which.files[1])

{

qc.outer<- III4e[identify( III4e, n=4), ]

test<-dist( rbind( data.matrix(rmeas), qc.outer))

dists<-diag(dist2full( test)[1:4, 5:8]) ### four distances

}

else

{

qc.outer<- I4e[identify( I4e, n=4), ]

test<-dist( rbind( data.matrix(rmeas), qc.outer))

dists<-diag(dist2full( test)[1:4, 5:8]) ### four distances

}

if(side.eye=='L') dists[c(2,1, 4,3)]<- dists

}


names(areas)<- c('III4e','I4e','I2e','blind spot')

names(dists)<- c('superior nasal','superior temporal',

                 'inferior temporal','inferior nasal')


mtext(side=3, line=2, paste('ID=',file.name,sep=''), cex=1.5)

title(sub=

cat( paste(names(areas), round(areas,1), sep=' = '), sep=' '))

print(' ',quote=FALSE)

invisible(c(round(areas,1), round(dists,2)) )#### output - 4
areas and 4 dists
```

```
} ### stops Goldmann


else ### starts Octopus

{

output.list<- list(III4e, I4e, I2e, blind, rmeas)

names(output.list)<- c('III4e','I4e','I2e','blind', 'rmeas')

print(output.list)


check.directory.exists(subDir='Octopus\\Octopus_processed')


for (i in 1:5)

{

   if(!is.null(output.list[[i]]))

   {

     mat.aux<- output.list[[i]]

     points(mat.aux[,1], mat.aux[,2],col=i, cex=1, pch=19)


               mat.aux2<- delete.points(mat.aux)

               print(mat.aux2)

               mat.aux3<- stop.identify(mat.aux2) ### ordered
list of chosen points

               print(mat.aux3)

               mat.aux3<-as.data.frame(mat.aux2[mat.aux3, ])
###

               names(mat.aux3)<-c('X','Y')

               write.csv(mat.aux3,

                file=paste('Octopus\\Octopus_processed',

                paste( file.name,'O',names(output.list)[i],

                '.csv', sep=''), sep='\\'),
```

```
                row.names=FALSE)

          output.list[[i]]<- mat.aux3

    }

}## closes the loop

invisible(output.list)

} ### closes if then else for deactivate.cleaning

}



goldmann.readWrite.data <-
function(name.input.file="Goldmann\\Goldmann_demographics.csv",

          name.output.file="Goldmann\\Goldmann results.csv",

          skip.reliability.meas=FALSE)

{

### this function compiles all cleaned Goldmann data

### returns a matrix of individual results (areas, etc)

### and writes a *.csv file


goldmann.demogr <- read.csv(name.input.file, header=TRUE)

names(goldmann.demogr)[1]<- 'ID'


b0<- (1:dim(goldmann.demogr)[1])[!is.na(goldmann.demogr$Eye)]

goldmann.demogr<- goldmann.demogr[b0,]


list.of.files<- paste(goldmann.demogr$ID,

substring(goldmann.demogr$Eye,1,1),sep='')


num.files<- length(list.of.files
```

```
### declare matrix for results

areas.goldmann<- matrix(NA, nrow=num.files,ncol=8) ### 8 refers
to 4 areas and 4 dists



for( i in 1:num.files)

{

print(list.of.files[i])

areas.goldmann[i,]<-

plot.individual(file.name=list.of.files[i],
dir.name='Goldmann\\Goldmann_data',

                skip.reliability.meas=skip.reliability.meas,
perimeter='G', deactivate.cleaning=TRUE)

}




dimnames(areas.goldmann)<- list( list.of.files,

      c('III4e','I4e','I2e','blind spot',

        'superior nasal','superior temporal',

        'inferior temporal','inferior nasal'))



### separate ID and side.eye

side.eye<- as.factor(substring( dimnames(areas.goldmann)[[1]],
6,6))

attr(side.eye, 'levels')<- c('R','L')



id<- as.character(as.factor(substring(
dimnames(areas.goldmann)[[1]], 1,5)))

attr(id, 'levels')<- substring( dimnames(areas.goldmann)[[1]],
1,5)
```

```
areas.goldmann<- cbind( id, side.eye, areas.goldmann)


write.csv(areas.goldmann, file=name.output.file,
row.names=FALSE, na='')


invisible(areas.goldmann)


}


octopus.readWrite.data <-
function(name.input.file="Octopus\\Octopus_demographics_.csv",
name.output.file="Octopus\\Regular24_test.csv",
skip.reliability.meas=FALSE)

{

### DP 17.10.13

### this function compiles all cleaned Octopus data

### returns a matrix of individual results (areas, etc)

### and writes a *.csv file


octopus.demogr <- read.csv(name.input.file, header=TRUE)

names(octopus.demogr)[1]<- 'ID'


b0<- (1:dim(octopus.demogr)[1])[!is.na(octopus.demogr$Eye)]

octopus.demogr<- octopus.demogr[b0,]


list.of.files<- paste(octopus.demogr$ID,

                      substring(octopus.demogr$Eye,1,1),sep='')


num.files<- length(list.of.files)
```

```
### declare matrix for results

areas.octopus<- matrix(NA, nrow=num.files,ncol=8) ### 8 refers
to 4 areas and 4 dists

for( i in 1:num.files)

{

print(list.of.files[i])

areas.octopus[i,]<-

plot.individual(file.name=list.of.files[i],
dir.name='Octopus\\Octopus_processed',

                skip.reliability.meas=skip.reliability.meas,

                perimeter='O', deactivate.cleaning=TRUE)

}



dimnames(areas.octopus)<- list( list.of.files,

      c('III4e','I4e','I2e','blind spot',

        'superior nasal','superior temporal',

        'inferior temporal','inferior nasal'))



### separate ID and side.eye

side.eye<- as.factor(substring( dimnames(areas.octopus)[[1]],
6,6))

attr(side.eye, 'levels')<- c('R','L')



id<- as.character(as.factor(substring(
dimnames(areas.octopus)[[1]], 1,5)))

attr(id, 'levels')<- substring( dimnames(areas.octopus)[[1]],
1,5)



areas.octopus<- cbind( id, side.eye, areas.octopus)
```

```
write.csv(areas.octopus, file=name.output.file,
row.names=FALSE, na='')


invisible(areas.octopus)


}

#################################################################
##############################

### Analysis functions

#################################################################
##############################


regular24<-

function(file.name, dir.name='Goldmann\\Goldmann_data')

{

### This function realigns individual points along 24 sectors


### file.name is the file name using format defined for studyid

### note that file.name only contains e.g. "M2005R"

### dir.name is the data directory name - assume it's below
getwd()

### output is a list with named elements "III4e" "I4e"   "I2e"
"blind"

### note that exactly one of the first three elements must be
NULL

### because...

### the output list is split by sector and isopter and

### contains the distance of each point to the origin and
frequencies in

### each sector (must be 0 or 1)
```

```
require(circular)

is.octopus<- substring(dir.name,1,1)=='O'

file0<- paste(dir.name, file.name,sep='\\')
file1<- paste(file0, 'GIII4e.csv', sep='')
file2<- paste(file0, 'GI4e.csv', sep='')
file3<- paste(file0, 'GI2e.csv', sep='')

if(is.octopus)
{
file0<- paste(dir.name, file.name,sep='\\')
file1<- paste(file0, 'OIII4e.csv', sep='')
file2<- paste(file0, 'OI4e.csv', sep='')
file3<- paste(file0, 'OI2e.csv', sep='')
}


which.files <-file.exists(c(file1, file2, file3))

isopter.names<-c('III4e','I4e','I2e')

III4e<- I4e<- I2e<-  NULL

if(which.files[1]) ### far outer
{
III4e<- read.csv(file1, header=TRUE)
```

```
}

if(which.files[2]) ### outer
I4e<- read.csv(file2, header=TRUE)

if(which.files[3]) ### innner
I2e<- read.csv(file3, header=TRUE)

side.eye<- substring(file.name, 6,6) ## must be L or R only

if(side.eye=='L')
{
if( which.files[1]) III4e[,1]<- -III4e[,1]
if( which.files[2]) I4e[,1]<- -I4e[,1]
if( which.files[3]) I2e[,1]<- -I2e[,1]

}

### compute distances

dIII4e<- dI4e<- dI2e<-  NULL

if(  which.files[1]) dIII4e<- apply( III4e, 1,
function(x){sqrt(sum(x^2))})
if(  which.files[2]) dI4e<- apply( I4e, 1,
function(x){sqrt(sum(x^2))})
if(  which.files[3]) dI2e<- apply( I2e, 1,
function(x){sqrt(sum(x^2))})
```

```
angIII4e<- angI4e<- angI2e<-  NULL


### transform coordinates to radians - use coord2rad from
library(circular) - uses atan2

### and returns an object of class circular


if( which.files[1]) angIII4e<- coord2rad(III4e)

if( which.files[2]) angI4e<- coord2rad(I4e)

if( which.files[3]) angI2e<- coord2rad(I2e)




df.angles<- list(angIII4e, angI4e, angI2e)

df.dist<- list( dIII4e, dI4e, dI2e)


### counts by sector


arcsM<- rad(seq( 0,  345, by=15)) ### angles for centra lines
of arcs

arcsL<- rad(c(352.5, seq(7.5, 337.5, by=15))) ### lower

arcsU<- rad( c( 7.5, seq(22.5, 352.5, by=15))) ### upper


positions<- dists<- freqs<- matrix(0, ncol=3, nrow=24)

dimnames(positions)<- dimnames(dists)<- dimnames(freqs)<-

        list( 1:24, c('III4e', 'I4e', 'I2e'))


length.dists<- unlist(lapply( df.dist, length))


for (i in 1:3) ### III4e, I4e, I2e
```

```
if( which.files[i] )

{

    pos.aux<- rep(0, length.dists[i]) ### initialises vector of
positions for each observation

    for (j in 1:24)  ### iterate over sectors

           {

                  if( j==1)

                       b0<- df.angles[[i]] <= arcsU[j] |
df.angles[[i]] > arcsL[j]

                    else

                       b0<- df.angles[[i]] <=arcsU[j] &
df.angles[[i]] > arcsL[j] ### find the index of observation in
sector j

                 if(sum(b0)>0) ### if the sector is not empty

                  {

                      if(sum(b0)>1)

                          {

                            print(paste('there are
',sum(b0),' points in sector ',j,

                                                ' of isopter
',isopter.names[i],

                                                ' in subject ',
file.name,sep=''),quote=FALSE)

                           positions[j,i]<- dists[j,i]<-
freqs[j,i]<-NA

                          }

                     else

                       {

                           positions[j,i]<-
(1:length.dists[i])[b0] ### observation in sector j

                           dists[j,i]<- df.dist[[i]][b0] ###
puts distance in obs determined by b0 in correct sector

                              if(j==1)
```

```
                                    freqs[j,i]<- freqs[j,i] +
sum(df.angles[[i]]<= arcsU[j] | df.angles[[i]] > arcsL[j])

                                else

                                    freqs[j,i]<- freqs[j,i] +
sum(df.angles[[i]]<= arcsU[j] & df.angles[[i]] > arcsL[j])

                            }

                }

            } ### close loop over sectors


}


### output is a list with elements distsance and frequencies

invisible(list( dists=dists, freqs=freqs))

}




do.regular24<-
function(name.input.file="Goldmann\\Goldmann_demographics.csv",

                        range.sex=NULL, range.age=NULL,
range.quality=NULL,

                        plot.isopter='III4e', CI.or.Quant='CI',

                        force23=FALSE,

                        name.output.file="Regular24_test.csv")

{

### This function completes the data sorting process

### It compiles all individual files into a matrix  specified
by

### sex, age and quality variables. This allows the user to
analyse data

### range.sex must be NULL (include all subjects), 'Female', or
'Male'
```

```
### range.age must be NULL (all ages), or a (numeric) a single
value or a vector of length 2 specifying a closed range

### range.quality must be NULL (all subjects),

###                   or a single value from {"Good witness",
"Fair witness", "Poor witness"}

###                   or a vector of length 2 from that set

### plot.isopter must be one of 'III4e', 'I4e', 'I2e'

### CI.or.Quant is either 'CI' or 'Quant' for 95% CI's or 95%
quantile envelope

### force23 is a binary indicator - FALSE to define the closure

###         of the bands at sectors 23 and 1; TRUE to define it
at sectors 23 and 2

###

### The graphic output of this function is just to visualise
data

### To get estimates and proper CI's use function quantile.fit



is.octopus<- substring(name.input.file,1,1)=='O'



goldmann.demogr <- read.csv(name.input.file, header=TRUE)

names(goldmann.demogr)[1]<- 'ID'



b0<- (1:dim(goldmann.demogr)[1])[!is.na(goldmann.demogr$Eye)]
### extracts positions individuals with data available

b00<-  !is.na(goldmann.demogr$Eye) ### logical - individuals
with meaningful data



if(!is.null(range.sex)) b0a<- b00 &
is.element(goldmann.demogr$Sex, range.sex)   else b0a<-
rep(TRUE, length(b00))

if(!is.null(range.age)) b0b<- b00 &
is.element(goldmann.demogr$Age, range.age)  else b0b<-
rep(TRUE, length(b00))
```

```
if(!is.null(range.quality)) b0c<- b00 &
is.element(goldmann.demogr$Quality.of.test, range.quality) else
b0c<- rep(TRUE, length(b00))



b00<- b0a & b0b & b0c



goldmann.demogr<- goldmann.demogr[b00,]  ### select filtered
individuals



list.of.files<- paste(goldmann.demogr$ID,
substring(goldmann.demogr$Eye,1,1),sep='') ### generates list
of files

num.files<- length(list.of.files)



### declare space for distances and frequencies over sectors

mat.output<- matrix(0, nrow=num.files*24, ncol=8) ### ncolo =
id, sector, dists x 3, freqs x 3



name.aux<- rep( list.of.files, rep( 24, num.files))

sec.aux<- rep(paste('S',1:24,sep=''), num.files)

names.aux<- paste( name.aux,sec.aux, sep='-')

names1<- c('III4e','I4e','I2e')

dimnames(mat.output)<- list(names.aux,

c('ID', 'Sector',paste('d',names1,sep=''),
paste('f',names1,sep='')))



mat.output[,2]<- rep(1:24, num.files)



k0<-0



if(is.octopus)
```

```
{

               for (i in list.of.files)
                                {
                                                k0<-k0+1
                                                s0<- seq(1 + (k0-
1)*24, k0*24)
                                                mat.output[s0,
1]<-rep(k0, 24)

                                                aux<- regular24(i,
dir.name='Octopus\\Octopus_processed')

                                                mat.output[s0,
3:5]<-aux$dists
                                                mat.output[s0,
6:8]<-aux$freqs
                                }

}

else

for (i in list.of.files)
{
   k0<-k0+1
   s0<- seq(1 + (k0-1)*24, k0*24)
   mat.output[s0, 1]<-rep(k0, 24)

   aux<- regular24(i)
```

```
   mat.output[s0, 3:5]<-aux$dists

   mat.output[s0, 6:8]<-aux$freqs

}


mat.output<- as.data.frame(mat.output)


mat.output$Sex<- rep( goldmann.demogr$Sex, rep( 24,num.files))

mat.output$Age<- rep( goldmann.demogr$Age, rep(24, num.files))

mat.output$Quality.of.test <- rep(
goldmann.demogr$Quality.of.test, rep( 24,num.files))


#####


arcsM<- rad(seq( 0,  345, by=15)) ### angles for centra lines
of arcs




ind.isopter<- switch(plot.isopter,  'III4e' = 3, 'I4e' =
4,'I2e' = 5)

col.isopter<- switch(plot.isopter,  'III4e' = 'black', 'I4e' =
'royalblue3', I2e' = 'maroon')


b1<- mat.output[, ind.isopter]>0


### get confidence intervals


if(CI.or.Quant == 'CI')

{
```

```
   test1<-tapply( mat.output[b1,ind.isopter], mat.output[b1,
'Sector'], mean)

   test2<-sqrt( tapply( mat.output[b1,ind.isopter],
mat.output[b1,'Sector'], var)) #sd



  if(min( mat.output[b1, 'Sector'] >1))

   {

      test1<- c( NA, test1)

      test2<- c( NA, test2)

   }

   inner<- cbind((test1 -1.96*test2)* cos(arcsM), (test1 -
1.96*test2)* sin(arcsM))

   outer<-  cbind((test1 +1.96*test2)* cos(arcsM), (test1
+1.96*test2)* sin(arcsM))

   middle<- cbind(test1*cos(arcsM), test1*sin(arcsM))




   ind.closure<-1

   if (is.na(inner[1,1]) | force23) ind.closure <- 2



    inner<- rbind( inner, inner[ind.closure,])

    middle<- rbind( middle, middle[ind.closure,])

    outer<- rbind( outer, outer[ind.closure,])



   set.template()

   if(force23)

   {

      lines(inner[-1,], col='firebrick4', lwd=2)

      lines(middle[-1,], col=col.isopter, lwd=2)

      lines(outer[-1,], col='firebrick4', lwd=2)
```

```
   }
   else
       {
      lines(inner, col=2, lwd=2)
      lines(outer, col=2, lwd=2)
      lines(middle, col=2, lwd=2)
       }

   x1<- c(outer[,1], rev(inner[,1]))
   y1<- c(outer[,2], rev(inner[,2]))

} ### end of CI procedure

else
{
#### get quantiles

   q1<- tapply( mat.output[b1,ind.isopter], mat.output[b1,
'Sector'], quantile,
            probs=c(0.025, 0.5, 0.975))

   q1<- matrix( unlist(q1), ncol=3, byrow=TRUE) ### ok

   if(min( mat.output[b1, 'Sector'] >1))  q1<- rbind(
rep(NA,3), q1) ### add 1st sector

   inner<- cbind( q1[,1]*cos(arcsM), q1[,1]*sin(arcsM))
   middle<- cbind( q1[,2]*cos(arcsM), q1[,2]*sin(arcsM))
   outer<- cbind( q1[,3]*cos(arcsM), q1[,3]*sin(arcsM))
```

```
    ind.closure<-1
    if (is.na(inner[1,1]) | force23) ind.closure <- 2



     inner<- rbind( inner, inner[ind.closure,])
     middle<- rbind( middle, middle[ind.closure,])
     outer<- rbind( outer, outer[ind.closure,])


    set.template()


    if(force23)
    {
       lines(inner[-1,], col='firebrick4', lwd=2)
       lines(middle[-1,], col=col.isopter, lwd=2)
       lines(outer[-1,], col='firebrick4', lwd=2)
    }
    else
    {
       lines(inner, col='firebrick4', lwd=2)
       lines(middle, col=col.isopter, lwd=2)
       lines(outer, col='firebrick4', lwd=2)
    }


    x1<- c(outer[,1], rev(inner[,1]))
    y1<- c(outer[,2], rev(inner[,2]))
} ### end of quantiles procedure
```

```
test<- polygon(x1, y1, col='snow3', density=36, border='grey')



if(force23)
   {
      lines(inner[-1,], col='firebrick4', lwd=2)
      lines(middle[-1,], col=col.isopter, lwd=2)
      lines(outer[-1,], col='firebrick4', lwd=2)
   }
   else
   {
      lines(inner, col='firebrick4', lwd=2)
      lines(middle, col=col.isopter, lwd=2)
      lines(outer, col='firebrick4', lwd=2)
   }



areas<- c(areapl( na.omit(inner)),
          areapl( na.omit(middle)),
                areapl( na.omit(outer))) ## frmom library
splancs
names( areas)<- c('inner','middle','outer')


####  change distances == 0 to NA's


for (i in 3:5) mat.output[,i]<- ifelse( mat.output[,i]==0, NA,
mat.output[,i])


### compute rose diagram of frequencies
```

```
mat.output<- as.data.frame(mat.output)


invisible(list(mat.output=mat.output,
regions=list(inner=inner,middle=middle,outer=outer),
areas=areas))


}




do.rose.diag<- function( Sector, freqs, shrink=1/2,
col='salmon', prop=1,

rotation=NULL)

{

### works with output from do.regular24

### constructs rose.diagram for frequencies per sector

###

warning("This function only runs after do.regular24 has been
run")

n.sectors<- max( Sector)

angle1<- 360/n.sectors

circ.freqs<- table( Sector, freqs)[,2]

angles<- angle1*(0:n.sectors)[-(n.sectors+1)]

vals.angles<- circular(rad( rotation+rep( angles, circ.freqs)),
units='radians',

                       template='none')

### radians transformed to circular object

rose.diag(vals.angles, bins=n.sectors,shrink=shrink, col=col,
prop=prop)

invisible( circ.freqs)

}
```

```
plot.all<- function( mat.output,names.isopter,

           plot.lines=TRUE, title1=' ')

{

### mat.output is part of the outcome of do.regular24

### isopter is the position of the isopter in mat.output

### isopter == 3 is III4e, 4 is I4e, and 5 is I2e

###

warning("This function only runs after do.regular24 has been
run")


arcsM<- rad(seq( 0,  345, by=15)) ### angles for centra lines
of arcs


ind.isopter<- ifelse(names.isopter=='III4e', 3,

              ifelse(names.isopter=='I4e', 4, 5))


xy<- cbind(

     mat.output[, ind.isopter]*cos(arcsM),

     mat.output[, ind.isopter]*sin(arcsM))


set.template()


title(main=title1)

if(!plot.lines)

{points(xy[,1], xy[,2])

id<- mat.output[, 1]
```

```
print(paste('There are ',length(unique(id)),' children',
sep=''),quote=FALSE)

}

else

{

k0<-0

id<- mat.output[, 1]

print(paste('There are ',length(unique(id)),' children',
sep=''),quote=FALSE)



for (i in unique( id))

    {

        k0<-k0+1

        b0<- i==id

        x0<- c(xy[b0,1], xy[b0,1][1])

        y0<- c(xy[b0,2], xy[b0,2][1])

        lines(x0,y0, col=k0, lwd=1)

     }

}

invisible(NULL)

}




quantile.fit<-
function(name.input.file="Goldmann\\Goldmann_demographics_06121
3.csv",

                        range.sex=NULL, range.age=NULL,
range.quality=NULL,

                        plot.isopter='III4e',
show.raw.data=FALSE, flip=FALSE,

                        tau=c(0.025, 0.25, 0.5, 0.75, 0.975))
```

```
{

### range.sex must be NULL (include all subjects), 'Female', or
'Male'

### range.age must be NULL (all ages), or a (numeric) a single
value or a vector of length 2 specifying a closed range

### range.quality must be NULL (all subjects),

###                   or a single value from {"Good witness",
"Fair witness", "Poor witness"}

###                   or a vector of length 2 from that set

### plot.isopter must be one of 'III4e', 'I4e', 'I2e'

###



require(lqmm)

is.octopus<- substring(name.input.file,1,1)=='O'




goldmann.demogr <- read.csv(name.input.file, header=TRUE)

names(goldmann.demogr)[1]<- 'ID'



b0<- (1:dim(goldmann.demogr)[1])[!is.na(goldmann.demogr$Eye)]
### extracts positions individuals with data available

b00<-  !is.na(goldmann.demogr$Eye) ### logical - individuals
with meaningful data



if(!is.null(range.sex)) b0a<- b00 &
is.element(goldmann.demogr$Sex, range.sex)   else b0a<-
rep(TRUE, length(b00))

if(!is.null(range.age)) b0b<- b00 &
is.element(goldmann.demogr$Age, range.age)  else b0b<-
rep(TRUE, length(b00))
```

```
if(!is.null(range.quality)) b0c<- b00 &
is.element(goldmann.demogr$Quality.of.test, range.quality) else
b0c<- rep(TRUE, length(b00))



b00<- b0a & b0b & b0c



goldmann.demogr<- goldmann.demogr[b00,]  ### select filtered
individuals



list.of.files<- paste(goldmann.demogr$ID,
substring(goldmann.demogr$Eye,1,1),sep='') ### generates list
of files

num.files<- length(list.of.files)



### declare space for distances and frequencies over sectors

mat.output<- matrix(0, nrow=num.files*24, ncol=8) ### ncolo =
id, sector, dists x 3, freqs x 3



name.aux<- rep( list.of.files, rep( 24, num.files))

sec.aux<- rep(paste('S',1:24,sep=''), num.files)

names.aux<- paste( name.aux,sec.aux, sep='-')

names1<- c('III4e','I4e','I2e')

dimnames(mat.output)<- list(names.aux,

c('ID', 'Sector',paste('d',names1,sep=''),
paste('f',names1,sep='')))



mat.output[,2]<- rep(1:24, num.files)



k0<-0



if(is.octopus)
```

```
{

       for (i in list.of.files)
              {
                     k0<-k0+1
                     s0<- seq(1 + (k0-1)*24, k0*24)
                     mat.output[s0, 1]<-rep(k0, 24)

                     aux<- regular24(i,
dir.name='Octopus\\Octopus_processed')

                     mat.output[s0, 3:5]<-aux$dists
                     mat.output[s0, 6:8]<-aux$freqs
              }

}

else

for (i in list.of.files)
{
   k0<-k0+1
   s0<- seq(1 + (k0-1)*24, k0*24)
   mat.output[s0, 1]<-rep(k0, 24)

   aux<- regular24(i)

   mat.output[s0, 3:5]<-aux$dists
   mat.output[s0, 6:8]<-aux$freqs
```

```
}


mat.output<- as.data.frame(mat.output)


mat.output$Sex<- rep( goldmann.demogr$Sex, rep( 24,num.files))

mat.output$Age<- rep( goldmann.demogr$Age, rep(24, num.files))

mat.output$Quality.of.test <- rep(
goldmann.demogr$Quality.of.test, rep( 24,num.files))

#print(mat.output)

#####


for (i in 3:5) mat.output[,i]<- ifelse( mat.output[,i]==0, NA,
mat.output[,i])


ind.isopter<- switch(plot.isopter,  'III4e' = 3, 'I4e' =
4,'I2e' = 5)

col.isopter<- switch(plot.isopter,  'III4e' = 'black', 'I4e' =
'royalblue3',

                                    'I2e' = 'maroon')


iso.band.col<- switch(plot.isopter,  'III4e' = 'gray45', 'I4e'
= 'gray45',

                                    'I2e' = 'gray45')


arcsM<- rad(seq( 0,  345, by=15)) ### angles for centra lines
of arcs


## To super-impose raw data points:

if(show.raw.data) plot.all(mat.output,
names.isopter=plot.isopter,

                           plot.lines=FALSE)
```

```
else(set.template())

if(plot.isopter =='III4e')
{

test<- mat.output[, c(1,2,3)]
test<-data.frame( ID=test$ID, theta=arcsM[test$Sector],
                  r=test$dIII4e)
}
if(plot.isopter =='I4e')
{

test<- mat.output[, c('ID','Sector', 'dI4e')]
test<-data.frame( ID=test$ID, theta=arcsM[test$Sector],
                  r=test$dI4e)
}

if(plot.isopter =='I2e')
{

test<- mat.output[, c('ID','Sector', 'dI2e')]
test<-data.frame( ID=test$ID, theta=arcsM[test$Sector],
                  r=test$dI2e)
}

arcsX<-seq( 0, 2*pi, length=1000) ## fine seq to predict
arcsX<- data.frame(theta=arcsX)
arcsX<- unlist(arcsX)
```

```
c1<- cos(arcsX)

s1<- sin(arcsX)


mod3<- lqmm(  r ~ cos( theta) + sin(theta) + cos(2*theta) +
sin(2*theta)

               + I(sin(theta)*cos(2*theta)), tau=tau,

               random= ~1, group=ID,  na.action=na.omit,

               data=test)


pred3<- matrix(NA, ncol=length(tau), nrow=length( arcsX))


for (i in 1:length(tau))

{

beta<- mod3$theta_x

pred3[,i] <- beta[1,i] + beta[2,i]*cos( arcsX) +
beta[3,i]*sin(arcsX) +

             beta[4,i]*cos(2*arcsX) + beta[5,i]*sin(2*arcsX) +

             beta[6,i]*sin(arcsX) * cos(2*arcsX)

}


if (!flip)

{


innerx<-  pred3[,1]*c1

innery<-  pred3[,1]*s1


outerx<- pred3[,5]*c1

outery<- pred3[,5]*s1
```

```
innerlx<- -innerx

outerlx<- -outerx


inner<- cbind(innerlx, innery)

outer<- cbind(outerlx, outery)




}

else


{

innerx<-  pred3[,1]*c1

innery<-  pred3[,1]*s1


outerx<- pred3[,5]*c1

outery<- pred3[,5]*s1


inner<- cbind(innerx, innery)

outer<- cbind(outerx, outery)


inner<- rbind( inner, inner)

outer<- rbind( outer, outer)


x1<- c(outer[,1], rev(inner[,1]))

y1<- c(outer[,2], rev(inner[,2]))


test<- polygon(x1, y1, col='snow3', density=36, border='grey')

}
```

```
for ( i in seq(10,70,by=10))

{

draw.circle( 0,0, radius=i,border='gray', nv=500)

text( 0, -i,  i, cex=2/3, col='slategray')

text( 0, i, i, cex=2/3, col='slategray')

text( -i,2, i, cex=2/3, col='slategray')

text(i,2,i,cex=2/3, col='slategray')

}


text(c(-80,-90,80,90),rep(2,4), rep(c(80,90),2),

cex=2/3, col='slategray')


text(par()$usr[1] -4, 0, "180", col='darkslategray',cex=3/5,
family='sans')

text(par()$usr[2] + 2, 0, "0", col='darkslategray',cex=3/5,
family='sans')


lines( pred3[,1]*c1, pred3[,1]*s1,lwd=2,col=iso.band.col,lty=1)

lines( pred3[,3]*c1, pred3[,3]*s1,lwd=3,col= col.isopter,lty=1)

lines( pred3[,5]*c1, pred3[,5]*s1,lwd=2,col=iso.band.col,lty=1)

lines( pred3[,2]*c1, pred3[,2]*s1,lwd=1,col='blueviolet',lty=2)

lines( pred3[,4]*c1, pred3[,4]*s1,lwd=1,col='blueviolet',lty=2)


}
```

9.7 Appendix VIII – kineticF package

The analytical functions developed were adapted for public use and published via the open-source repository CRAN. All CRAN submissions are assessed by a team of programmers before publication. `kineticF` is available from https://cran.r-project.org/web/packages/kineticF/index.html .

The website information and `kineticF` user guide are appended below.

`kineticF: Framework for the Analysis of Kinetic Visual Field Data`

Data cleaning, processing, visualisation and analysis for manual (Goldmann) and automated (Octopus 900) kinetic visual field data.

Version:	1.0
Depends:	R (> 3.1.0)
Imports:	circular, lqmm, splancs, sp, plotrix, MASS
Published:	2015-06-04
Author:	Dipesh E Patel & Mario Cortina-Borja
Maintainer:	Dipesh E Patel <dipesh_patel at ucl.ac.uk>
License:	GPL-2 | GPL-3 [expanded from: GPL (≥ 2)]
NeedsCompilation:	no
CRAN checks:	kineticF results
Downloads:	

Reference manual:	kineticF.pdf
Package source:	kineticF_1.0.tar.gz
Windows binaries:	r-devel: kineticF_1.0.zip, r-release: kineticF_1.0.zip, r-oldrel: kineticF_1.0.zip
OS X Snow Leopard binaries:	r-release: kineticF_1.0.tgz, r-oldrel: not available
OS X Mavericks binaries:	r-release: kineticF_1.0.tgz

Package 'kineticF'

June 4, 2015

Type Package

Title Framework for the Analysis of Kinetic Visual Field Data

Version 1.0

Depends R(> 3.1.0)

Imports circular, lqmm, splancs, sp, plotrix, MASS

Date 2015-06-04

Author Dipesh E Patel & Mario Cortina-Borja

Maintainer Dipesh E Patel <dipesh_patel@ucl.ac.uk>

Description Data cleaning, processing, visualisation and analysis for manual (Goldmann) and automated (Octopus 900) kinetic visual field data.

License GPL (>= 2)

NeedsCompilation no

LazyData true

Repository CRAN

Date/Publication 2015-06-04 17:32:34

R topics documented:

`kineticF-package` *Framework for the Analysis of Kinetic Visual Field Data*

Description

A collection of functions covering data cleaning, processing, visualisation and analysis for manual (Goldmann) and automated (Octopus 900) kinetic visual field data. The analysis is primarily aimed at summarising normative data, with code provided to allow programmers to adapt the basic functions to their specific needs.

Details

Package:	kineticF
Type:	Package
Version:	1.0
Date:	2015-06-04
License:	GPL (>= 2)

Author(s)

Dipesh E Patel <dipesh_patel@ucl.ac.uk> and Mario Cortina-Borja <m.cortina@ucl.ac.uk>

`delete.points` *Removal of unwanted points from a kinetic isopter*

Description

Deletes unwanted (practice or error) points from a kinetic isopter. Only called by function `kFsubj` to clean files when `perimeter = 'O'`. This assumes that all Goldmann data have been cleaned and ordered at the point of digitisation. This function is for internal use and is not meant to be called by the user.

Usage

```
delete.points(outer.iso)
```

Arguments

`outer.iso`	A matrix of coordinates

Value

matrix of coordinates excluding deleted points

Author(s)

Dipesh E Patel & Mario Cortina-Borja

dist2full *Distance structure to full symmetric matrix*

Description

Creates a symmetric distance matrix from a lower triangular vector structure. It is used to calculate distances within other functions. This function is for internal use and is not meant to be called by the user.

Usage

```
dist2full(dis)
```

Arguments

dis	a distance structure

Value

a full symmetric matrix of distances

References

Becker, R.A.; Chambers, J.M. (1984). *S: An Interactive Environment for Data Analysis and Graphics.* Pacific Grove, CA, USA: Wadsworth & Brooks/Cole. ISBN 0-534-03313-X.

do.rose.diag *Rose diagrams of sector frequencies*

Description

Generates rose diagrams from sector frequencies and thus can only be called after calling `kf.sort`.

Usage

```
do.rose.diag(Sector, freqs, shrink = 1/2, col = "salmon", prop = 1,
             rotation = NULL)
```

Arguments

Sector	numeric, vector of sector values
freqs	numeric, vector of frequencies of values within each sector
shrink	parameter that controls the size of the plotted circle. Default is 1. Larger values shrink the circle, while smaller values enlarge the circle
col	character, fill colour
prop	numerical constant determining the radii of the sectors. By default, `prop = 1`
rotation	numeric, angle of rotation

Value

figure	Rose diagram graphical output
circ.freqs	numeric, vector of aggregated frequencies in 24 sectors

Author(s)

Dipesh E Patel & Mario Cortina-Borja

References

rose.diag{circular}

Examples

```
## kf.sort must be run before do.rose.diag

test<- kf.sort()

try3<- do.rose.diag(test$mat.output$Sector, test$mat.output$fIII4e,
                    shrink=0.9, prop=2.5, col='salmon', rotation=0)

mtext(text='III4e points plotted', side=3, line=-18, cex=1.2)
```

---

gcomp *Input and output of Goldmann data*

Description

Populates a matrix containing all cleaned individual Goldmann area and KPRM data.

Usage

```
gcomp(inf = NULL, perimeter = "G", no.kprm = TRUE)
```

Arguments

inf	name of the demographics matrix used
perimeter	character, to remain as "G"
no.kprm	logical, TRUE if no kinetic perimetry reliability measure (KPRM) has been used

Value

matrix containing information on ID, eye tested and areas

Author(s)

Dipesh E Patel & Mario Cortina-Borja

Examples

```
## Not run:
gcomp()
## End(Not run)
```

`Goldmann.demogr` *Goldmann demographics*

Description

A matrix of subject demographics for Goldmann perimetry. Called with analysis functions.

Usage

```
data("Goldmann.demogr")
```

Format

A data frame with 2 observations on the following 5 variables:

`Study.ID.No.` a factor with levels on Study ID

`Eye` a factor with levels `Left` and `Right`

`Sex` a factor with levels `Male` and `Female`

`Age` a numeric vector

`Quality.of.test` a factor with levels `Good witness`, `Fair witness` and `Poor witness`

Details

This sample matrix demonstrates the required demographics format to the user.

Source

DEP and MCB

Examples

```
data(Goldmann.demogr)
```

kf.sector *Point extraction into 24 sectors*

Description

Extracts coordinate data from an individual dataset into sectors (every 15 degrees) and distances (from origin).

Usage

```
kf.sector(file.name, is.octopus = FALSE)
```

Arguments

file.name	file name using format defined for study ID and eye designation (either "R" or "L")
is.octopus	logical, TRUE if Octopus perimeter has been used

Value

matrix containing sectors, frequencies and distances

Author(s)

Dipesh E Patel & Mario Cortina-Borja

Examples

```
kf.sector('M0001R', is.octopus=TRUE)
```

kf.sort *Visualisation of summary statistics*

Description

Plots summary statistics to aid data visualisation.

Usage

```
kf.sort(inf = NULL, is.octopus = FALSE, range.sex = NULL,
        range.age = NULL, range.qual = NULL, plot.isopter = "III4e",
    CI.or.Quant = "CI", force23 = TRUE)
```

Arguments

inf	name of the demographics matrix used
is.octopus	logical, TRUE if Octopus perimeter has been used
range.sex	character, either NULL (use all data) or "Male" or "Female"
range.age	numeric, either NULL (use all data) or single value or a vector of length 2 specifying a closed age range
range.qual	character, either NULL (use all data) or a single value from "Good witness", "Fair witness", "Poor witness"
plot.isopter	character, "III4e", "I4e", or "I2e"
CI.or.Quant	character, either "CI" or "Quant" for 95% CI"s or 95% quantile envelope
force23	logical, FALSE to define the closure of the bands at sectors 23 and 1; TRUE to define it at sectors 23 and 2

Value

mat.output	data.frame, containing 24 rows (sectors) for each individual with columns: ID, sector, dists x 3, freqs x 3 (corresponding to 3 isopters)
regions	list with elements, inner, middle and outer - matrices containing coordinates of output statistics
areas	character, vector of area values defined by output statistics

Author(s)

Dipesh E Patel & Mario Cortina-Borja

Examples

```
kf.sort()
```

---

kFcheck *Visualisation of isopter values*

Description

Plots curves or points for multiple individuals on a kinetic grid

Usage

```
kFcheck(mat.output, name.iso, plot.lines = TRUE, title1 = " ")
```

Arguments

mat.output	data.frame generated by kf.sort
name.iso	character, one of "III4e", "I4e" or "I2e"
plot.lines	logical, if TRUE individual isopters are plotted, otherwise individual data points are displayed
title1	character, specifying plot title

Value

Graphical output

Author(s)

Dipesh E Patel & Mario Cortina-Borja

Examples

```
## Only runs after kf.sort has run
test3<- kf.sort()
kFcheck(test3$mat.output, "III4e", title1="III4e data", plot.lines=FALSE)
```

---

kFquant *Quantile regression modelling of kinetic field data*

Description

Fits quantile regression models to kinetic field data and displays predicted isopter values for selected quantiles. Used to generate normative/control isopter values.

Usage

```
kFquant(inf = NULL, is.octopus = FALSE, range.sex = NULL,
        range.age = NULL, range.qual = NULL, plot.iso = "III4e",
    show.raw = FALSE, tau = c(0.025, 0.25, 0.5, 0.75, 0.975))
```

Arguments

inf	character, name of the demographics matrix
is.octopus	logical, TRUE if Octopus perimeter data
range.sex	character, either NULL (use all data) or "Male" or "Female"
range.age	numeric, either NULL (use all data) or single value or a vector of length 2 specifying a closed age range
range.qual	character, either NULL (use all data) or a single value from "Good witness", "Fair witness", "Poor witness"
plot.iso	character, "III4e", "I4e", or "I2e"

show.raw	logical, superimpose raw data points on grid? Default is FALSE.
tau	numeric, vector of quantiles to be fitted. Default is 5%, 25%, 50%, 75% and 95%.

Value

Graphical output

Author(s)

Dipesh E Patel & Mario Cortina-Borja

References

Geraci, M and Bottai, M. (2014) Linear quantile mixed models. *Statistics and Computing*, **24(3)**, 461-479. doi: 10.1007/s11222-013-9381-9.

Examples

```
## This requires sufficient data to generate robust models

kf.sort()
kFquant(range.qual="Good witness", range.age= 8:400,
        plot.iso="III4e", show.raw=FALSE)
```

---

kFsubj *Plots a subject's kinetic data*

Description

Displays Goldmann and Octopus perimetry data. Octopus data can also be cleaned and re-ordered by this function. Isopter area values are calculated and displayed.

Usage

```
kFsubj(obj.name, perimeter = "G", no.cleaning = TRUE, no.kprm = TRUE, no.flip = TRUE)
```

Arguments

obj.name	object (subject) name using format defined for study ID - (please note: ID can only be 5 characters in length)
perimeter	either character, "G" (Goldmann) or "O" (Octopus)
no.cleaning	logical, TRUE if data have been cleaned and ordered
no.kprm	logical, TRUE if no kinetic perimetry reliability measure (KPRM) has been used
no.flip	logical, if FALSE, function displays mirror image along the y-axis for left-eye data

Value

Graphical output of isopters and list of values

Author(s)

Dipesh E Patel & Mario Cortina-Borja

Examples

```
data(Goldmann.demogr, package='kineticF', envir = environment())
data(M0001RGIII4e, package='kineticF', envir = environment())
data(M0001RGI4e, package='kineticF', envir = environment())
data(M0001RGblind, package='kineticF', envir = environment())
test<- kFsubj(obj.name='M0001R', perimeter='G',
              no.cleaning=TRUE,
              no.kprm=TRUE, no.flip=TRUE)
```

M0001Oraw *Octopus raw data*

Description

Sample data. Simulates Octopus raw .txt file string for subject 1.

Usage

```
data("M0001Oraw")
```

Format

A text string

Details

This dataset assumes a direct export from an Octopus 900 perimeter.

Source

DEP and MCB

Examples

```
data(M0001Oraw)
```

M0001RGblind *Goldmann raw data*

Description

Sample data. Goldmann blind spot data for subject 1.

Usage

```
data("M0001RGblind")
```

Format

A data frame with 7 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0001RGblind)
```

M0001RGI4e *Goldmann raw data*

Description

Sample data. Goldmann isopter I4e data for subject 1.

Usage

```
data("M0001RGI4e")
```

Format

A data frame with 15 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0001RGI4e)
```

`M0001RGIII4e` *Goldmann raw data*

Description

Sample data. Goldmann isopter III4e data for subject 1.

Usage

```
data("M0001RGIII4e")
```

Format

A data frame with 16 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0001RGIII4e)
```

M0001ROblindproc *Octopus processed data*

Description

Sample data. Octopus blind spot data for subject 1, that is cleaned and ordered, ready for analysis.

Usage

```
data("M0001ROblindproc")
```

Format

A data frame with 8 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0001ROblindproc)
```

M0001ROblindraw *Octopus unprocessed data*

Description

Sample data. Octopus blind spot data for subject 1, that requires cleaning and ordering, before analysis.

Usage

```
data("M0001ROblindraw")
```

Format

A data frame with 10 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0001ROblindraw)
```

`M0001ROI4eproc` *Octopus processed data*

Description

Sample data. Octopus isopter I4e data for subject 1, that is cleaned and ordered, ready for analysis.

Usage

```
data("M0001ROI4eproc")
```

Format

A data frame with 17 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0001ROI4eproc)
```

M0001ROI4eraw *Octopus unprocessed data*

Description

Sample data. Octopus isopter I4e data for subject 1, that requires cleaning and ordering, before analysis.

Usage

```
data("M0001ROI4eraw")
```

Format

A data frame with 17 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0001ROI4eraw)
```

M0001ROIII4eproc *Octopus processed data*

Description

Sample data. Octopus isopter III4e data for subject 1, that is cleaned and ordered, ready for analysis.

Usage

```
data("M0001ROIII4eproc")
```

Format

A data frame with 19 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0001ROIII4eproc)
```

`M0001ROIII4eraw` *Octopus unprocessed data*

Description

Sample data. Octopus isopter III4e data for subject 1, that requires cleaning and ordering, before analysis.

Usage

```
data("M0001ROIII4eraw")
```

Format

A data frame with 23 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0001ROIII4eraw)
```

M0002LGblind *Goldmann raw data*

Description

Sample data. Goldmann blind spot data for subject 2.

Usage

```
data("M0002LGblind")
```

Format

A data frame with 8 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0002LGblind)
```

M0002LGI2e *Goldmann raw data*

Description

Sample data. Goldmann isopter I2e data for subject 2.

Usage

```
data("M0002LGI2e")
```

Format

A data frame with 24 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0002LGI2e)
```

`M0002LGI4e` *Goldmann raw data*

Description

Sample data. Goldmann isopter I4e data for subject 2.

Usage

```
data("M0002LGI4e")
```

Format

A data frame with 24 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0002LGI4e)
```

M0002LOblindproc *Octopus processed data*

Description

Sample data. Octopus blind spot data for subject 2, that is cleaned and ordered, ready for analysis.

Usage

```
data("M0002LOblindproc")
```

Format

A data frame with 7 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0002LOblindproc)
```

M0002LOblindraw *Octopus unprocessed data*

Description

Sample data. Octopus blind spot data for subject 2, that requires cleaning and ordering, before analysis.

Usage

```
data("M0002LOblindraw")
```

Format

A data frame with 7 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0002LOblindraw)
```

`M0002LOI2eproc` *Octopus processed data*

Description

Sample data. Octopus isopter I2e data for subject 2, that is cleaned and ordered, ready for analysis.

Usage

```
data("M0002LOI2eproc")
```

Format

A data frame with 14 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0002LOI2eproc)
```

M0002LOI2eraw *Octopus unprocessed data*

Description

Sample data. Octopus isopter I2e data for subject 1, that requires cleaning and ordering, before analysis.

Usage

```
data("M0002LOI2eraw")
```

Format

A data frame with 17 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0002LOI2eraw)
```

M0002LOI4eproc *Octopus processed data*

Description

Sample data. Octopus isopter I4e data for subject 2, that is cleaned and ordered, ready for analysis.

Usage

```
data("M0002LOI4eproc")
```

Format

A data frame with 16 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0002LOI4eproc)
```

`M0002LOI4eraw` *Octopus unprocessed data*

Description

Sample data. Octopus isopter I4e data for subject 2, that requires cleaning and ordering, before analysis.

Usage

```
data("M0002LOI4eraw")
```

Format

A data frame with 21 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0002LOI4eraw)
```

M0002Oraw *Octopus raw data*

Description

Sample data. Simulates Octopus raw .txt file string for subject 2.

Usage

```
data("M0002Oraw")
```

Format

A text string

Details

This dataset assumes a direct export from an Octopus 900 perimeter.

Source

DEP and MCB

Examples

```
data(M0002Oraw)
```

M0003RGIII4e *Goldmann raw data*

Description

Sample data. Goldmann isopter III4e data for subject 3.

Usage

```
data("M0003RGIII4e")
```

Format

A data frame with 23 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0003RGIII4e)
```

`M0004LGIII4e` *Goldmann raw data*

Description

Sample data. Goldmann isopter III4e data for subject 4.

Usage

```
data("M0004LGIII4e")
```

Format

A data frame with 13 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0004LGIII4e)
```

M0005RGIII4e *Goldmann raw data*

Description

Sample data. Goldmann isopter III4e data for subject 5.

Usage

```
data("M0005RGIII4e")
```

Format

A data frame with 23 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0005RGIII4e)
```

M0005RGrmeas *Goldmann raw data*

Description

Sample data. Goldmann Kinetic Perimetry Reliability Measure (KPRM) data for subject 5.

Usage

```
data("M0005RGrmeas")
```

Format

A data frame with 4 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0005RGrmeas)
```

`M0006RGIII4e` *Goldmann raw data*

Description

Sample data. Goldmann isopter III4e data for subject 6.

Usage

```
data("M0006RGIII4e")
```

Format

A data frame with 18 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0006RGIII4e)
```

M0007LGIII4e *Goldmann raw data*

Description

Sample data. Goldmann isopter III4e data for subject 7.

Usage

```
data("M0007LGIII4e")
```

Format

A data frame with 23 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0007LGIII4e)
```

M0008RGIII4e *Goldmann raw data*

Description

Sample data. Goldmann isopter III4e data for subject 8.

Usage

```
data("M0008RGIII4e")
```

Format

A data frame with 23 observations on the following 2 variables.

`X` a numeric vector, the x co-ordinate value

`Y` a numeric vector, the y co-ordinate value

Source

DEP and MCB

Examples

```
data(M0008RGIII4e)
```

---

ocomp *Input and output of Octopus data*

Description

Populates a matrix containing all cleaned individual Octopus area and KPRM data.

Usage

```
ocomp(inf = NULL, no.kprm = TRUE, perimeter = "O")
```

Arguments

inf	name of the demographics matrix used
no.kprm	logical, TRUE if no kinetic perimetry reliability measure (KPRM) has been used
perimeter	character, either "G" or "O"

Value

matrix containing information on ID, eye tested and areas

Author(s)

Dipesh E Patel & Mario Cortina-Borja

Examples

```
## Not run:
ocomp(no.kprm=TRUE)

## End(Not run)
```

Octopus.demogr *Octopus demographics*

Description

A sample matrix of subject demographics for Octopus perimetry. Called with analysis functions.

Usage

```
data("Octopus.demogr")
```

Format

A data frame with 2 observations on the following 5 variables.

`Study.ID.No.` a factor with levels `M0001` `M0002`

`Eye` a factor with levels `Left` and `Right`

`Sex` a factor with levels `Male` and `Female`

`Age` a numeric vector

`Quality.of.test` a factor with levels `Good witness`, `Fair witness` and `Poor witness`

Details

This sample matrix demonstrates the required demographics format to the user.

Source

DEP and MCB

Examples

```
data(Octopus.demogr)
```

preprocess.octopus *Octopus data cleaner*

Description

Transforms text strings into coordinate values by isopters, one subject at a time. NOTE: For this function to run, a demographics file must exist (columns: Study ID No, Eye, Sex, Age, Quality of test). Only subjects with values on at least Study ID No and Eye can be processed.

Usage

```
preprocess.octopus(octopus.file, octopus.demogr = Octopus.demogr)
```

Arguments

octopus.file	name of the matrix containing individual raw data text string
octopus.demogr	name of the demographics matrix

Value

Matrix of coordinates and isopter values

Author(s)

Dipesh E Patel & Mario Cortina-Borja

Examples

```
## For example, import raw data with:
# M0001Oraw<- paste(scan("C:\\Data\\Octopus_raw\\M0001.txt", sep=';', what=''), collapse=';')

preprocess.octopus(M0001Oraw)
```

---

set.template *Kinetic visual field template*

Description

Opens a plot window and displays a kinetic perimetry grid

Usage

```
set.template(void = TRUE)
```

Arguments

void	Adds the 'void' areas of a Goldmann field to the kinetic plot. Default is TRUE.

Value

Graphical output

Author(s)

Dipesh E Patel & Mario Cortina-Borja

Examples

```
set.template(void=FALSE)
```

`stop.identify` *Stops the process of re-ordering a matrix of coordinates*

Description

Changes the order in which a matrix of coordinates is plotted to allow closure on a polygon. This function is for internal use and is not meant to be called by the user.

Usage

```
stop.identify(xy)
```

Arguments

`xy`	matrix of coordinates

Value

A re-ordered matrix of coordinates

Author(s)

Dipesh E Patel & Mario Cortina-Borja

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9.8 Appendix VII – Outputs

9.8.1 Peer-reviewed papers

Patel, DE; Cumberland, PM; Russell-Eggitt, I; Walters, BC; Rahi, JS on behalf of the OPTIC study group. Study of Optimal Perimetric Testing In Children (OPTIC): Feasibility, reliability and repeatability of perimetry in children. **PLoS One** 2015;10(6):e0130895. doi: 10.1371/journal.pone.0130895

Patel, DE; Cumberland, PM; Russell-Eggitt, I; Walters, BC; Cortina-Borja, M; Rahi, JS on behalf of the OPTIC study group. Study of Optimal Perimetric Testing In Children (OPTIC): Normative visual field values in children. **Ophthalmology**. 2015;122(8):1711-7. doi: 10.1016/j.ophtha.2015.04.038

Patel, DE; Geraci, M; Cortina-Borja M. Modelling normative kinetic perimetry isopters using mixed-effects quantile regression. **Journal of Vision**. 2016;16(6):7, 1–6. doi:10.1167/16.6.7.

Patel, DE; Viswanathan, AC; Garway-Heath, DF; Cumberland, PM; Walters, BC; Russell-Eggitt, I; Cortina-Borja, M; Rahi, JS on behalf of the OPTIC study group. Study of Optimal Perimetric Testing In Children (OPTIC): Development and feasibility of the Kinetic Perimetry Reliability Measure (KPRM). **BJO**. In press.

PLOS | ONE

RESEARCH ARTICLE

Study of Optimal Perimetric Testing in Children (OPTIC): Feasibility, Reliability and Repeatability of Perimetry in Children

Dipesh E. Patel[1,2,3,4], Phillippa M. Cumberland[1,2], Bronwen C. Walters[4,2], Isabelle Russell-Eggitt[2], Jugnoo S. Rahi[1,2,3,4,5]*, OPTIC study group[¶]

1 Life Course Epidemiology and Biostatistics Section, UCL Institute of Child Health, London, United Kingdom, **2** Ulverscroft Vision Research Group, London, United Kingdom, **3** Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom, **4** Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom, **5** UCL Institute of Ophthalmology, London, United Kingdom

¶ OPTIC study group members are listed in the Acknowledgments.
* j.rahi@ucl.ac.uk

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Data Availability Statement: Due to ethical restrictions on data sharing related to participant consent, aggregated data are available upon request to Professor Jugnoo Rahi (j.rahi@ucl.ac.uk).

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Abstract

Purpose

To investigate feasibility, reliability and repeatability of perimetry in children.

Methods

A prospective, observational study recruiting 154 children aged 5–15 years, without an ophthalmic condition that affects the visual field (controls), identified consecutively between May 2012 and November 2013 from hospital eye clinics. Perimetry was undertaken in a single sitting, with standardised protocols, in a randomised order using the Humphrey static (SITA 24–2 FAST), Goldmann and Octopus kinetic perimeters. Data collected included test duration, subjective experience and test quality (incorporating examiner ratings on comprehension of instructions, fatigue, response to visual and auditory stimuli, concentration and co-operation) to assess feasibility and reliability. Testing was repeated within 6 months to assess repeatability.

Results

Overall feasibility was very high (Goldmann=96.1%, Octopus=89% and Humphrey=100% completed the tests). Examiner rated reliability was 'good' in 125 (81.2%) children for Goldmann, 100 (64.9%) for Octopus and 98 (63.6%) for Humphrey perimetry. Goldmann perimetry was the most reliable method in children under 9 years of age. Reliability improved with increasing age (multinomial logistic regression (Goldmann, Octopus and Humphrey), $p<0.001$). No significant differences were found for any of the three test strategies when examining initial and follow-up data outputs (Bland-Altman plots, $n=43$), suggesting good test repeatability, although the sample size may preclude detection of a small learning effect.

scheme. Phillippa Cumberland is supported by the Ulverscroft Foundation and Jugnoo Rahi receives a proportion of her funding from the NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology. The funders and sponsors had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. An Octopus perimeter was loaned to Great Ormond Street Hospital by Haag-Streit (AG, Switzerland) for use in this study.

Competing Interests: The authors have the following financial declarations: An Octopus perimeter was loaned to Great Ormond Street Hospital by Haag-Streit (AG, Switzerland) for use in this study. This does not alter the authors' adherence to PLOS ONE policies on sharing data and materials.

Conclusions

Feasibility and reliability of formal perimetry in children improves with age. By the age of 9 years, all the strategies used here were highly feasible and reliable. Clinical assessment of the visual field is achievable in children as young as 5 years, and should be considered where visual field loss is suspected. Since Goldmann perimetry is the most effective strategy in children aged 5–8 years and this perimeter is no longer available, further research is required on a suitable alternative for this age group.

Introduction

Visual field (VF) testing is a key parameter in assessing and monitoring visual function in patients with ophthalmic and neurological diseases[1]. It is estimated that over 3500 children under 16 years of age undergo formal perimetry in the UK per year[2], without any consensus on approaches in children. There is also a paucity of robust data on the correct interpretation of these tests, in particular on reliability, to inform understanding of the usefulness of perimetry in monitoring children.

To date, a number of small studies have investigated perimetry in children without ophthalmic conditions[3–10], generally using methods and algorithms not commonly available/utilised in routine clinical practice. Variation in findings relating to test feasibility and reliability reflects the diversity of testing strategies.

In UK hospitals, the Humphrey SITA algorithms and Goldmann perimetry (no longer commercially available) are the two most common perimetric approaches in children with suspected/confirmed VF loss[2]. Prior studies have tested feasibility of Goldmann perimetry using single isopters with large stimuli (i.e. V4e or III4e) along limited test meridians, limiting their ability to inform clinical practice[9–12]. Semi-automated kinetic perimetry (Octopus 900) is reported to be feasible in children[13]. However there is no evidence regarding its comparative feasibility and reliability, which is necessary to understand whether the Octopus can reliably replace the Goldmann as the perimeter of choice in children.

The SITA algorithms are some of the shortest threshold tests available[11] and children are able to perform shorter static algorithms more reliably than longer tests[14, 15], with the SITA Fast and Standard algorithms having equivalent precision for detecting VF progression[16]. Assessment of reliability in static perimetry currently relies on the use of automated indices (false positives, fixation losses, and false negatives) despite evidence reported in adults that reproducibility (the gold-standard measure of reliability) is not associated with any of these measures[17]. Thus assessment of reliability and subsequent interpretation of results in children using static perimetry is currently unknown.

There is therefore a limited evidence base on which clinicians can draw to decide which perimetric technique to use, how to assess test reliability and interpret the findings accounting for subject age. As part of a larger programme of research investigating the role of paediatric perimetry, we report here an investigation of feasibility, reliability, and repeatability of common perimetric tests in children. Specifically, we compared Octopus automated kinetic perimetry with the current 'gold-standard' Goldmann kinetic perimetry.

Methods

Participants (described in Table 1) were recruited consecutively from patients and their siblings attending Moorfields Eye Hospital, London, reflecting the broader patient population of children who might require visual field testing as part of their clinical care. Parents or legal guardians gave written consent for participation and children gave verbal assent. Ophthalmic diagnosis, visual acuity and refractive state were extracted from clinical case notes. Children without medical records (siblings of patients) underwent a full Orthoptic examination, including focimetry where appropriate.

Assessments were performed using an Octopus 900 (Haag-Streit AG, Switzerland), a Humphrey Visual Field Analyzer 750i (Carl Zeiss Meditec VG mbH, Germany) and a Goldmann perimeter (Haag-Streit, Bern, Switzerland). All tests were carried out by an experienced Orthoptist (DEP) in the same visual field testing room fitted with a blackout blind and using regularly calibrated perimeters. Assessments were undertaken in a randomised order (assigned by a random number generator, Microsoft Excel 2010), with short rest periods between tests. In children with unilateral amblyopia, the non-amblyopic eye was tested. For those with good acuity in each eye, and no strabismus/treated amblyopia, one eye was randomly selected and tested.

At the start of the session, the participant sat on a height adjustable chair and he/she was shown the relevant perimeter prior to testing and was given an explanation of the test procedure. This involved instructions to fix centrally and press their buzzer every time a light was perceived (either a flash or moving light dependent on the perimeter). He/she was also given an opportunity to test the buzzer. All instructions were delivered in age appropriate language. The child then had the non-tested eye occluded with a soft eye pad, was set up at the perimeter, and seat and chin rest adjustments were made until the position was correct and he/she felt comfortable. Additional padding on the chinrest to reach the correct height was given to any participant requiring it. Significant refractive errors were corrected using large aperture lenses for the I2e stimulus and static perimetry only using criterion modified from Henson[18]: $\geq$ +3.00 dioptre spheres (DS), $\geq$ -1.00DS, $>$ ±1.00 dioptre cylinders (DC). The time taken to prepare the participant was recorded and a note was made of any modifications necessary to perform the assessment. Encouragement and repetition of instructions were given throughout the tests. Participants were offered a rest break during the test if they appeared to be getting tired/losing concentration and if taken, this was recorded by the examiner.

Kinetic visual field assessments

Both the Goldmann and Octopus kinetic perimetry assessments were performed using the same testing protocol, adapted from Werner[19]. Assessments started with three practice

Table 1. Inclusion/exclusion criteria for participants.

Inclusion Criteria
Children aged 5 to 15 years
No history of ophthalmological disease that could cause a visual field defect, but including children with refractive error, unilateral amblyopia and strabismus, where the fellow (normal) eye was to be tested. No prior experience of perimetry.
Visual acuity of 0.2 LogMAR or better (20/32 Snellen equivalent) in the tested eye
Exclusion Criteria
Children with any impairments, such as severe learning disability, which would make co-operation with formal perimetry challenging
Children not accompanied by a parent or legal guardian

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presentations with the first test isopter allowing familiarisation with the test procedure. These were not used to form the test isopter. Targets were then presented along 12 cardinal meridian (every 30° in a pre-defined order), centripetally from a non-seeing area. Test points were started at manually plotted locations on the Octopus, with an automated speed of 5°/sec[13].

After plotting the 12 cardinal points, additional points were tested, in those children able to tolerate more extensive testing, in a non-randomised order along meridians 15° adjacent to the cardinal points starting with temporal field locations. This effectively 'filled-in' areas with larger distances between test points first, and allowed for more accurate plotting of visual field shape, up to a maximum of 24 points per isopter. Two isopters were plotted, to replicate common clinical practice and avoid overburdening participants, the choice being randomised between III4e, I4e and I2e.

Participants were asked to "sit back and relax" between isopters, allowing for a very short rest (generally less than 20 seconds). During this period they were shown the next test stimulus and then re-positioned to continue with the assessment.

The test procedure started with plotting an outer isopter, followed by inner isopter and then finally the plotting of the blind spot, with the I2e stimulus (stimulus speed of 2°/sec). This allowed children to get accustomed to testing using an easier stimulus, and allowed children to relate to an increased difficulty between isopters as "moving on to the next level."

Test points were re-plotted if the examiner felt the initial response was unreliable, to allow for temporary lapses in concentration and co-operation, without masking persistently limited co-operation.

Humphrey static perimetry assessment

Participants were assessed with the SITA 24–2 FAST algorithm. Gaze-tracking and blind spot monitoring were attempted using the Heijl-Krakau method.

Participants were specifically warned the lights could be "really bright or quite hard to see" during this test and were told when they were halfway through the algorithm.

Examiner Based Assessment of Reliability (EBAR)

Participants were rated on each perimetric assessment using an Examiner Based Assessment of Reliability (EBAR) scoring system developed for this study. The EBAR score is a qualitative, categorical system with outcomes of 'good', 'fair' or 'poor' quality of perimetric test. It is independent of visual field outcome. The EBAR rating was designed and implemented to guide the evaluation of reliability in paediatric perimetry. Participants were assigned a score using the criteria in Table 2.

Table 2. Examiner Based Assessment of Reliability (EBAR) scoring system.

'Good' rating: Compliance with testing is good. The participant is able to maintain good central fixation and respond promptly. They may have some fixation losses at times, but are able to understand and comply well with test instructions. General behaviour allows a comprehensive assessment and overall, visual field outcome is expected to represent true visual field size/sensitivity.
'Fair' rating: Compliance with testing is mostly good. The participant may have moderate fixation losses with some variability in responses. They are able to understand test instructions and their general behaviour allows for moderate co-operation. They may show evidence of fatigue that affects performance and respond to the noise of stimulus presentation at times. Overall, visual field outcome is expected to be able to detect gross defects, but may over/under-estimate true visual field size/sensitivity.
'Poor' rating: Compliance with testing is poor. The participant demonstrates very high fixation losses or searching for stimuli. They may be unable to ignore the sound of stimulus presentation and therefore produce high false positive responses. They may also demonstrate highly variable responses, with a possible lack of understanding of test instructions. Overall, test performance is not expected to represent true visual field size/sensitivity and results will be unable to rule-in or rule-out visual field defects.

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The time taken for each perimetric assessment, any modifications required, use of an additional chinrest or the need for rest breaks during the assessment were noted. Subjects who found it difficult to keep their chin resting at the perimeter were supported to keep their heads in position, but it did not impact on EBAR rating unless associated with other factors (e.g. poor concentration).

Assessment of subjective experience of perimetry

Participants rated how difficult they found each assessment, using a 5-point Likert scale ranging from 'Very Hard' to 'Very Easy'. Any other comments were recorded verbatim.

Follow-up examination

All participants were invited to return for a repeat examination within 6 months of the original testing to investigate repeatability. All repeat procedures were carried out in the same manner and order as the initial test.

Statistical methods

Raw data were extracted from the Humphrey perimeter using R code developed at City University (personal communication: Richard Russell) (The R Project for Statistical Computing (R v3.0.3, www.r-project.org)). Raw Goldmann and Octopus data were compiled using the R package'`kineticF`'[20] (R v3.1.2, www.r-project.org/).

Paper records completed by the examiner were entered into the database software REDCap [21] (Research Electronic Data Capture) hosted securely at UCL Institute of Child Health. All other analyses were performed in STATA (StataCorp. 2011. *Stata Statistical Software*: *Release 12*. College Station, TX: StataCorp LP). All left eye data were mirrored along the y-axis to represent right eye data for analysis. Chi-squared tests, linear and multinomial logistic regression analyses were undertaken.

The study was approved by the National Health Service Research Ethics Committee for London—Bloomsbury and followed the tenets of the Declaration of Helsinki.

Results

One hundred and fifty-four participants (Table 3) were tested between May 2012 and November 2013 from 348 eligible participants (44.3%). Of these, 43 (27.9%) returned for a follow-up visit.

Most (n = 93, 60.4%) were aged 5 to 8 years and 118/154 (76.6%) were White, with 9.7% Indian, 8.4% Black and 5.2% of mixed ethnicity. Those declining to participate were of similar ethnicity and age to those participating.

Table 3. Participant demographics and test feasibility for all perimeters (n = 154).

Age group (years)	Sex		Number completing assessments (%)			Mean test duration* (min) (SD)		
	Male	*Female*	*Goldmann*	*Octopus*	*Humphrey*	*Goldmann*	*Octopus*	*Humphrey*
5–6	22	18	36 (90)	32 (80)	40 (100)	9.2 (1.9)	9.1 (1.44)	7 (1.3)
7–8	23	30	51 (96.2)	48 (90.6)	53 (100)	9.4 (1.8)	9.1 (1.8)	6.2 (1.0)
9–11	13	22	35 (100)	32 (91.4)	35 (100)	9.3 (1.3)	8.5 (1.0)	5 (1.0)
12–15	15	11	26 (100)	25 (96.2)	26 (100)	8.6 (1.1)	8 (0.9)	4.6 (0.7)

*Test duration values include preparation and assessment tasks

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Median refractive error was 0.00D (spherical equivalent) IQR = 0D to +2.50D, range = -10.00 to +6.75D. 56/154 (36.4%) participants had strabismus, and 35/154 (22.7%) had unilateral amblyopia. Unless otherwise stated, reliability refers to results from EBAR (subjective examiner) scoring.

Feasibility of perimetry in children

No child had to stop testing completely due to fatigue or an unwillingness to continue with the assessment. All 3 perimetric tests were highly feasible for all ages (Table 3).

Increasing test quality (from 'poor' to 'good' quality) reduced test duration for all three perimeters (Goldmann ($p<0.001$), Octopus ($p = 0.035$), and Humphrey ($p<0.001$)).

For Octopus and Humphrey perimetry, 13/154 (8.4%) children, all under 8 years of age, required the use of additional chinrest support for correct positioning at the perimeter. Only 1/154 (0.7%) child required modifications to be successfully aligned for Goldmann perimetry (sat up on knees to reach the required height). Only 8/154 (5.2%) of all children showed visible signs of fatigue for Humphrey perimetry compared to 13/154 (8.4%) performing Goldmann and 19/154 (12.3%) performing Octopus assessments. No child above 9 years was affected by fatigue for Goldmann and Humphrey perimetry. Only 1/154 (0.7%) child, aged 7 years, required a break during Goldmann perimetry, with 4/154 (2.6%) and 9/154 (5.8%) requiring breaks for Octopus and Humphrey perimetry respectively.

For all isopters on both kinetic perimeters, there was a statistically significant increase in the number of points that could be plotted per isopter with age ($p<0.0001$) (Fig 1).

Reliability of perimetry in children

Fig 2 demonstrates the change in the proportion of 'good' EBAR ratings (test quality) with age for each perimetric assessment. Only Goldmann perimetry had >50% of tests rated as 'good' for children aged 5–6 years but test reliability improved with age for all perimeters ($p<0.0001$).

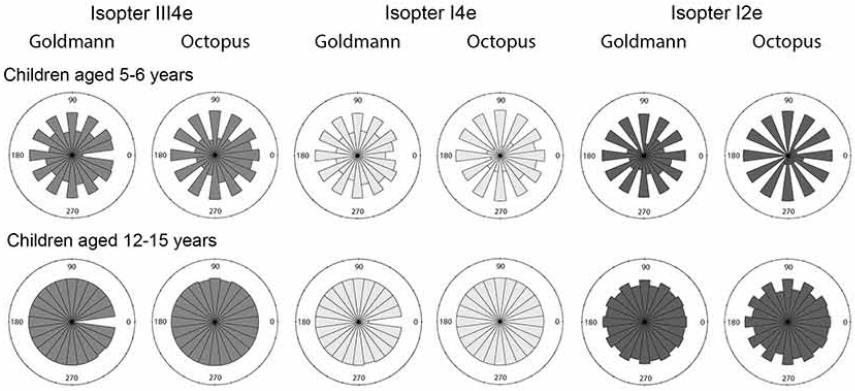

Fig 1. Rose diagrams of the frequency of points plotted along individual meridians for Goldmann and Octopus perimetry for children aged 5–6 years compared to 12–15 years. A larger area indicates a meridian with a larger number of plotted points. **The empty sectors at 0° for Goldmann perimetry isopters III4e and I4e correspond to the 'void' area in the perimeter bowl.*

doi:10.1371/journal.pone.0130895.g001

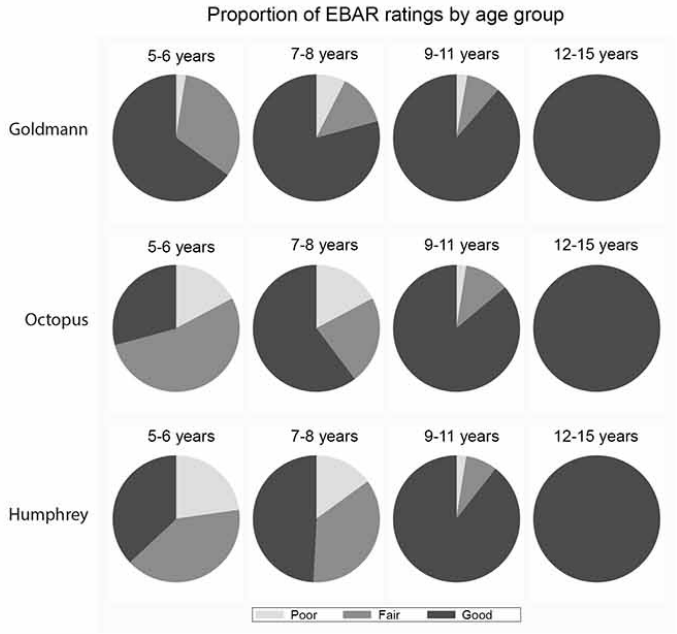

Fig 2. Proportion of EBAR (test quality) ratings per perimeter, by age groups.

doi:10.1371/journal.pone.0130895.g002

By ages 7–8 years there is a shift from large proportions of 'fair' tests to 'good' quality tests. In children over 9 years of age, no significant difference was found between Goldmann and Humphrey assessments (χ^2, $p = 0.123$).

Traditional reliability indices (RI) (fixation losses $\geq$ 25% or false positives $\geq$15%, as recorded by the Humphrey perimeter) indicated a large number of assessments (125/154 (81.2%)) would be classified as unreliable. Traditional RI's disagreed with EBAR in 74/154 cases (48.1%) (Table 4) i.e. 72 (good rating & unreliable RI) + 2 (poor rating & reliable RI). Splitting the two variables that compose the reliability index shows that fixation losses alone show a similar pattern of unreliability, and poor agreement with EBAR (test for trend; $p = 0.196$). However, only 42/154 (27%) assessments would be classified as unreliable using false positives alone and there is better agreement with EBAR, (test for trend; $p<0.001$), with only 17/154 (11%) assessments showing disagreement.

Examiner report showed in 16/154 (10.4%) (Goldmann) and 45/154 (29.2%) (Octopus) children it was not possible to reliably plot the blind spot. Of these 10/16 (62.5%) and 23/45 (51.1%) had tests rated 'fair' or 'poor' quality for Goldmann and Octopus respectively.

Participants reported testing with the Humphrey perimeter to be the most difficult (24.2% rated as difficult) and with the Goldmann to be the easiest (63.3% rated as easy). No relationship

Table 4. Comparison of Examiner Based Assessment of Reliability (EBAR) with automated reliability indices for Humphrey perimetry.

EBAR Rating	False Positives		Fixation Losses		Traditional Reliability Indices*	
	<15%	*≥15%*	*<25%*	*≥25%*	*Reliable*	*Unreliable*
Good	87	11	30	68	26	72
Fair	19	19	1	37	1	37
Poor	6	12	6	12	2	16
Total	112	42 (27%)	37	117 (76%)	29	125 (81%)

*Traditional reliability indices are defined here as fixation losses ≥ 25% or false positives ≥15%

doi:10.1371/journal.pone.0130895.t004

was found between subjective experience of test difficulty and examiner-rated test quality (Goldmann ($p = 0.305$), Octopus ($p = 0.146$) and Humphrey ($p = 0.166$)).

Notably, 39/154 (25.3%) of all children, mostly those aged ≤8 years (33/39), commented on, or responded to, the audible noise of stimulus presentation for Octopus perimetry. Of these, 17 (11% of the total sample) were reported by the examiner to have impacted on test quality. Verbatim responses from 33/154 (21.4%) participants using Humphrey perimetry were categorised and showed factors such as the rapid rate of stimulus presentation, the effect of testing to threshold (lots of stimuli that were difficult to see), and the varying locations of stimuli to be responsible for perceived difficulty.

Repeatability of perimetry in children

43/154 (27.9%) of children returned for a repeat assessment within 6 months of the original test with a mean follow-up time of 108 days (SD = 42). The follow-up sample had a similar age distribution to the initial sample (children aged 5–6 years ($n = 16$), 7–8 years ($n = 13$), 9–11 years ($n = 7$) and 12–15 years ($n = 7$)).

Bland-Altman plots of Goldmann and Octopus isopter areas for children with 'good' quality tests at both visits were performed and there were no statistically significantly differences found for any isopter, indicating good test repeatability on both perimeters (S1 Fig).

No significant difference in Humphrey perimetry mean deviation (MD) values were found between the two visits (Bland-Altman, Mean difference = -0.24dB (95%CI: [-3.6, 0.7]).

Discussion

We report that good quality perimetry is feasible in children as young as 5 years, although the prospects of achieving a reliable test improve with increasing age. Goldmann perimetry is the most reliable form of testing up to 9 years of age, but there appear to be no differences in reliability between test strategies above this age. Reliable tests are reproducible on repeat testing. Older children are able to plot more detailed kinetic assessments, allowing for better delineation of isopter shape.

Currently, there are no standardised methods for scoring test reliability in kinetic perimetry —for adults or children. The development and use of a new qualitative score here (EBAR) allows for assessment of reliability in kinetic perimetry, as well as providing information complementary to automated indices from static perimetry. EBAR can also be compared to participants' perception of test difficulty in children.

The lack of relationship between participants' perceived test difficulty and test reliability underlines the importance of encouraging children through tasks they perceive as difficult. Static perimetry (SITA 24–2 FAST) was the shortest test used here, yet had the poorest

reliability in young children and participant responses identified the intensity of the task as a potential cause of this.

Fatigue is known to impact on test reliability and outcomes[22]. For static perimetry (with threshold algorithms) this affects the accuracy of the entire test, whereas points plotted by kinetic perimetry before the onset of fatigue will still provide useful data. Thus, in a child who tires quickly, or struggles with intensive testing, plotting a baseline kinetic field can give valuable information on visual field sensitivity that cannot be achieved by static techniques. Our data suggest it is possible to find a balance between performing the test quickly (minimising fatigue) and ensuring children do not feel overwhelmed by the task.

Our protocols are suitable for use in a clinical setting, combining short familiarisation tasks and commonly available tests. By careful positioning[23], familiarising, and engaging the participant with the task[24], we were able to maximise the potential for a reliable result even in children as young as 5 years. Assessments were performed by a single, experienced examiner, and test feasibility and duration reflect this. Clinically, it is anticipated that children requiring visual field tests would be examined by clinicians experienced in performing perimetry in children. Our data also addressed gaps in the literature relating to the limits for number of points plotted per isopter (in kinetic perimetry) [11].

A small subset of participants returned for follow-up review, precluding our ability to assess repeatability in depth. However, we found 'good' results to be consistent (reproducible), and thus useful for indicating a change in visual field result occurring from a true change in sensitivity. It is expected that test reproducibility would differ if test quality varied between tests, and as such, these analyses are not presented. As with any study assessing subjective responses in children, our study was designed to capture as much relevant data in a single sitting without reducing the data quality from fatigue, or inducing sampling bias by use of protocols that subjects/families would be unwilling to undertake. Our data on children without visual field loss preclude our ability to comment specifically on test duration in the context of major field loss, which can be anticipated to require longer assessment [25]. Assessing three VF tests in one visit allowed for a greater breadth of comparisons but limited the testing to one eye. Nevertheless, we report here the largest systematic study of feasibility and reliability of perimetry in children assessing three key approaches.

We are unable to make direct comparisons with prior studies using Goldmann perimetry, as these have used 12 test points (4 meridian—repeated twice), with a mean test duration of 5.1 minutes[9] or have tested along 8 meridian with one isopter (mean duration = 11.06 min)[11]. This considerable variation reported in test duration with similar protocols highlights the potential influence of examiner experience in manual perimetry. We used a highly detailed protocol yet the mean test duration for Goldmann perimetry was 9.2 minutes (SD = 1.6) and 8.8 minutes (SD = 1.5) for Octopus perimetry, indicating that detail and quality can be achieved with a child-appropriate test duration.

A recent report on Octopus perimetry in children using a detailed test protocol has shown that, as children struggled to plot a blind spot, only 64% of those aged 10–12 years could plot reliable fields[13]. This contrasts with our study, in which children demonstrated better reliability. This may reflect the more nuanced assessment of reliability we used, compared to the pre-defined metrics of others, but could also reflect variation in assessment protocols between studies. There is very little evidence on repeatability of VF testing in children. The Behavioural Visual Field Test (BEFIE) is a screening test developed specifically for use in children. A large, longitudinal, retrospective study of this technique has shown that a proportion of children with VF defects show changes in sensitivity (including improvement) that are presumed to be learning/developmental effects[26]. Both our study and another[13] found no evidence of a significant 'learning effect'. However, as it would be reasonable to expect some learning effects,

especially with younger children and differentially in those with field defects as opposed to those with normal fields, this issue requires further investigation.

Visual field tests are a valuable diagnostic tool but are only one facet of a clinical examination, and care should be taken not to over/under-value individual test results[27]. Formal perimetry should be attempted in children with suspected VF loss and we suggest the reliability of these assessments can be documented using the EBAR scoring system we have developed, so that judgements can be made as to whether test results reflect true visual field sensitivity. The sole use of automated reliability measures for Humphrey static perimetry may lead to potentially useful results being disregarded and our data suggest false positive data can be combined with an EBAR score to better grade the reliability of individual test outputs.

For those children where formal perimetry is not possible, child-specific novel assessments have been suggested. These consist of supra-threshold tests using eye-tracking[28], or using modified perimeters[5]. Other techniques use game-based[29] or behavioural engagement[26]. These allow for a degree of quantification, but many of these require specialist equipment and are likely to only be performed in specialist centres.

Goldmann, Octopus and Humphrey perimetry are highly feasible in children, with Goldmann perimetry being the most reliable test in participants under 9 years of age. Above this age, all methods were highly reliable and normative, age-appropriate data exist for each perimetric technique[30]. Thus, the choice of perimetric technique should be informed by the clinical context of individual cases. The evidence base on repeatability remains incomplete and warrants further investigation to inform understanding of how to reliably rule-in/rule-out small but clinically significant changes in visual fields in children over time.

Supporting Information

S1 Fig. Bland-Altman plots of initial vs. follow-up visual field area. Bland-Altman plots of initial vs. follow-up visual field area for all isopters using Goldmann and Octopus perimetry. (PDF)

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OPTIC study group members: Peng Tee Khaw, Bronwen Walters, Phillippa Cumberland, Isabelle Russell-Eggitt, Chris Timms, John Brookes, Anthony Moore, Maria Papadopoulos, David Garway-Heath, Ananth Viswanathan, Alki Liasis, David Crabb, Mario Cortina-Borja, Dipesh Patel, and Jugnoo Rahi.

Author Contributions

Conceived and designed the experiments: DEP PMC BCW IRE JSR. Performed the experiments: DEP. Analyzed the data: DEP PMC. Contributed reagents/materials/analysis tools: DEP PMC BCW IRE JSR. Wrote the paper: DEP PMC BCW IRE JSR.

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Study of Optimal Perimetric Testing In Children (OPTIC)

Normative Visual Field Values in Children

*Dipesh E. Patel, BMedSci, PGDip,[1,2,3,4] Phillippa M. Cumberland, BA, MSc,[1,2] Bronwen C. Walters, BMedSci,[2,4] Isabelle Russell-Eggitt, FRCOphth,[2] Mario Cortina-Borja, MSc, PhD,[6] Jugnoo S. Rahi, PhD, FRCOphth,[1,2,3,4,5] for the OPTIC Study Group**

Purpose: We sought to define normative visual field (VF) values for children using common clinical test protocols for kinetic and static perimetry.

Design: Prospective, observational study.

Subjects: We recruited 154 children aged 5 to 15 years without any ophthalmic condition that would affect the VF (controls) from pediatric clinics at Moorfields Eye Hospital.

Methods: Children performed perimetric assessments in a randomized order using Goldmann and Octopus kinetic perimetry, and Humphrey static perimetry (Swedish Interactive Thresholding Algorithm [SITA] 24-2 FAST), in a single sitting, using standardized clinical protocols, with assessment by a single examiner. Unreliable results (assessed qualitatively) were excluded from the normative data analysis. Linear, piecewise, and quantile mixed-effects regression models were used. We developed a method to display age-specific normative isopters graphically on a VF plot to aid interpretation.

Main Outcome Measures: Summary measures and graphical plots describing normative VF data for 3 common perimetric tests.

Results: Visual field area increased with age on testing with Goldmann isopters III4e, I4e, and I2e (linear regression; $P < 0.001$) and for Octopus isopters III4e and I4e (linear regression; $P < 0.005$). Visual field development occurs predominately in the inferotemporal field. Humphrey mean deviation (MD) showed an increase of 0.3 decibels (dB; 95% CI, 0.21−0.40) MD per year up to 12 years of age, when adult MD values were reached and thereafter maintained.

Conclusions: Visual field size and sensitivity increase with age in patterns that are specific to the perimetric approach used. These developmental changes should be accounted for when interpreting perimetric test results in children, particularly when monitoring change over time. *Ophthalmology 2015;122:1711-1717 © 2015 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Supplemental material is available at www.aaojournal.org.

Perimetry is an important tool in the diagnosis and management of ophthalmic disease. Interpretation of findings relies on an understanding of the normal visual field (VF; i.e., reference values), its natural development and progression throughout the life-course,[1] and the variability of responses in normal subjects.[2] However, there is limited literature in all these areas with respect to children.

Newly developed algorithms for static perimeters undergo extensive testing and normative data are collected, against which test subjects are compared. However, such studies are based on adult subjects, so only adult reference data are available.[2] The effects of testing children and mapping their data to an adult reference are poorly understood, and findings differ according to the test algorithm and examination technique used.[3,4] Thus, there is little guidance available on interpretation of VF data in children, particularly for common static test strategies.

Although the extent of the VF has been reported for Goldmann perimetry in children (currently the "clinical−standard" kinetic measure), the use of large stimuli (V4e and III4e) and sparse test locations limit the clinical application of these existing data.[5,6] The Goldmann perimeter is no longer available commercially, and only 1 study[7] has produced normative isopter area values in children using a kinetic perimeter with similar specifications, namely, the Octopus 900 (n = 82; aged 5−15 years). Furthermore, the development of normative isopter models should account for the nonparametric distribution of points, yet current normative values (in adults and children) have failed to do this.[1,3,4]

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Previous studies have been inconsistent regarding maturation of VFs,[8–13] reflecting the diversity of assessment strategies, procedures, and small sample sizes. The most common tests performed in children in the UK are Goldmann and Humphrey (Swedish Interactive Thresholding Algorithm [SITA]) perimetry.[14] There is some evidence to suggest children without ocular pathology do not reach adult-level sensitivities with the SITA strategy, but reference values are not known.[6]

We report a systematic investigation of fields using Goldmann and Octopus kinetic, and Humphrey static perimetry (SITA 24-2 FAST), in children aged 5 to 15 years, attained using test protocols suitable for a clinical setting.

Methods

Participants were recruited consecutively from patients known to have disorders that do not impact on VFs attending Moorfields Eye Hospital, London, and their siblings. Where disorders were unilateral, the fellow (unaffected) eye was assessed. Informed, written consent was obtained from parents/legal guardians, and child participants gave verbal assent. To assess eligibility, information on diagnosis, visual acuity, and refractive status was obtained from clinical case notes or for those without medical records (siblings) a full Orthoptic examination, including focimetry where appropriate, was carried out. Table 1 shows the inclusion and exclusion criteria.

Perimetry was performed using a Goldmann perimeter (Haag-Streit, Bern, Switzerland), an Octopus 900 (Haag-Streit), and a Humphrey Visual Field Analyzer 750i (Carl Zeiss Meditec V, Jena, Germany). All tests were carried out in a randomized order (assigned by a pseudorandom number generator; Microsoft Excel 2010, Microsoft, Inc, Redmond, WA), by an experienced orthoptist (D.E.P.) in a dedicated perimetry room, using regularly calibrated perimeters. Children with unilateral amblyopia had their nonamblyopic eye tested and for those with bilateral good acuity and no strabismus/treated amblyopia, 1 eye was tested randomly.

Before testing, participants were made comfortable, familiarized with each perimeter, and given an explanation of the procedure using age-appropriate language. Testing was undertaken in clinical conditions, with a short rest period between tests (approximately 2–3 minutes). Test quality, judged by the examiner using the Examiner Based Assessment of Reliability scoring system, was scored as good, fair, or poor. This system accounts for factors affecting test quality, such as fixation, concentration, behavior, response to auditory stimuli, and fatigue. Data were collected to aid reporting of feasibility and reliability of testing (details reported elsewhere). Significant refractive errors (REs) were corrected using large aperture lenses for the I2e stimulus and static perimetry only using criterion modified from Henson[15]: $\geq+3.00$ diopter spheres, ≥-1.00 diopter spheres, $>\pm1.00$ diopter cylinders.

Kinetic Visual Field Assessments

The familiarization task comprised 3 presentations of the first test isopter. Practice points were not used to form the test isopter. For the test, targets were presented along 12 cardinal meridian (every 30° in a predefined order), centripetally from a nonseeing area using the testing protocol adapted from Werner.[16] Test points were started at manually plotted locations on the Octopus, with an automated speed of 5°/s.[7]

For those children who could tolerate further testing, additional points were tested, in a nonrandomized order along meridians 15° adjacent to the cardinal points starting with temporal field locations. This "filling in" between test points allowed for more accurate plotting of VF shape, up to a maximum of 24 points per isopter. Two isopters were plotted, randomly selected from III4e, I4e, or I2e. The test procedure started with plotting an outer isopter, followed by inner isopter and then finally the plotting of the blind spot, with the I2e stimulus (at a speed of 2°/s).

Test points were replotted if the examiner felt the initial response was unreliable, that is, the child lost fixation during the stimulus presentation, searched for stimuli, failed to respond, or pressed for the noise of stimulus presentation. This accommodated temporary lapses in cooperation, but ensured repeat testing was not undertaken in those with persistently poor cooperation.

Humphrey Static Perimetry Assessment

Participants were assessed with the SITA 24-2 FAST algorithm with gaze tracking and blind spot monitoring using the Heijl-Krakau method. Participants were warned the lights could be "really bright or quite hard to see" during this test and were told when they reached the midpoint of the test.

Statistical Methods

Manual perimetry results were scanned and digitized using Engauge digitizer software (open-source; available at: www.digitizer.sourceforge.net) with raw data point values stored in .csv files (Microsoft Excel 2010). Linear and piecewise models were fitted in Stata (StataCorp; 2011: Stata Statistical Software: Release 12. College Station, TX).

The association between mean deviation (MD) and age was modeled as a piecewise linear relationship, where initially a nonlinear least-squares estimation for frequency of MD with age was used to identify the optimum split point of age. Linear associations of age with MD were then fitted and reported separately, before and after the split point.

Raw kinetic perimetry data were exported from the Octopus perimeter and data points extracted using the R package kineticF[17] (The R Project for Statistical Computing, R v3.1.2; available at: www.r-project.org) designed for this purpose. Normative kinetic data were modeled using the linear quantile mixed-effects

Table 1. Inclusion and Exclusion Criteria for Participants

Inclusion criteria
Children aged 5–15 years.
No history of ophthalmologic disease that could cause a visual field defect, but including children with refractive error, unilateral amblyopia and strabismus, where the fellow (nonamblyopic) eye was to be tested. No prior experience of perimetry.
Visual acuity of $\geq$0.2 logarithm of the minimum angle of resolution (6/9.5 Snellen equivalent) in the tested eye.
Exclusion Criteria
Children with any impairments, such as severe learning disability, which would make cooperation with formal perimetry challenging.
Children not accompanied by a parent or legal guardian.

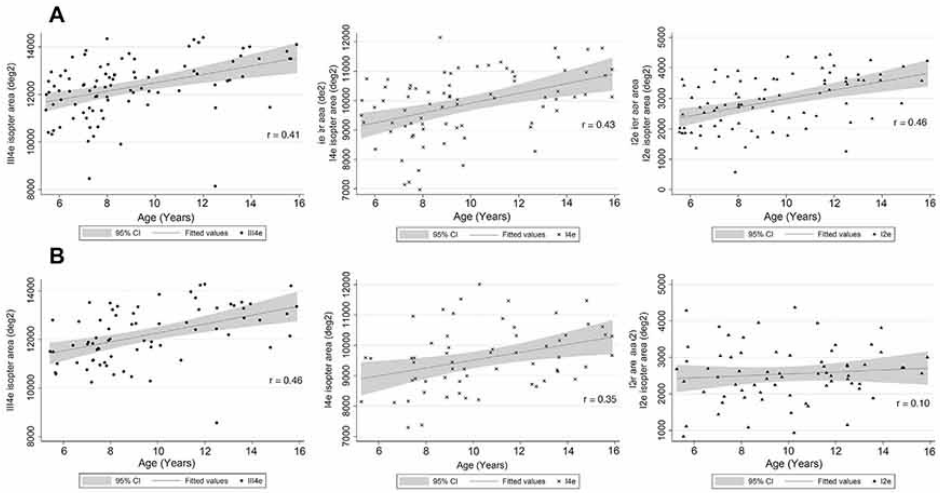

Figure 1. **A**, Goldmann visual field (VF) area versus age for isopters III4e, I4e, and I2e. **B**, Octopus VF area versus age for isopters III4e, I4e, and I2e. CI = confidence interval.

regression package lqmm[18] in R (version 3.0.1). This method allows fitting of distribution-free models to individual-clustered data that significantly departs from normality, and was used in the normative model in kineticF to summarize isopter distributions.[17,19] The model developed is described in detail in Appendix 1 (available at www.aaojournal.org).

Raw data were extracted from the Humphrey perimeter using R code developed at City University (Richard Russell, personal communication, January 2013). All left eye data were mirrored along the *y*-axis to represent right eye data for analysis.

The study was approved by the National Health Service Research Ethics Committee for London − Bloomsbury and followed the tenets of the Declaration of Helsinki.

Results

Between May 2012 and November 2013, 154 participants were recruited from 348 eligible subjects (44.3%). Of the 194 potentially eligible subjects who did not participate, 132 (68%) did not respond to the initial invitation, 34 (17.5%) declined, and 28 (14.4%) agreed but subsequently failed to attend for their assessment. Among the 34 eligible patients who declined to participate, 23 cited time constraints and 11 a lack of interest in contributing to research as the most common reasons. Participants and nonparticipants were of similar age and ethnicity distribution. The median age of participants was 8.0 years (interquartile range, 7.0−11.0) with 81 (52.6%) females (Appendix 2; available at www.aaojournal.org). Of the 154 in the sample, 118 (76.6%) were white, 9.7% Indian, 8.4% black, and 5.2% of mixed ethnicity.

Median RE was 0.0 diopters (D; spherical equivalent; interquartile range, 0−2.5 D; range, −10.00 to +6.75 D). Four subjects (2.6%) had an RE of >−5 D, 9 (5.9%) had >+5 D, and 141 (91.6%) had an RE between ±5 D. Of the 154 participants, 56 (36.4%) had strabismus, and 35 (22.7%) had unilateral amblyopia. Only 1 child (aged 5 years) was tested in a previously amblyopic eye but, owing to poor test quality, these data were not used to generate normative data (for full details, see Appendices 3 and 4, available at www.aaojournal.org). Only data from tests rated as "good" quality (by examiner rating) for reliability were included in the analysis of normative data, that is, those tests performed to a level that would give results representative of true VF sensitivity (Goldmann, n = 125 [81.2%]; Octopus, n = 100 [64.9%]; Humphrey, n = 98 [63.6%]), rather than cases where lack of cooperation affected results.

Kinetic Perimetry

Visual field area and age were fitted to linear regression models for both perimeters and each isopter (Fig 1). Model coefficients of 176.7 (III4e; 95% CI, 93.8−259.5), 167.3 (I4e; 95% CI, 86.4−248.2), and 141.7 (I2e; 95% CI, 80.9−202.5) were found for Goldmann isopters. These represent the change in area (square degrees) for each additional year of age from 5 to 15

Table 2. Octopus Perimetry Isopter Areas

Age Group (y)	Mean (SD) Isopter area (deg^2)		
	III4e	*I4e*	*I2e*
5−6	11 426 (806)	8854 (837)	2463 (996)
7−8	11 867 (977)	9213 (1084)	2518 (856)
9−11	12 627 (1140)	9843 (1149)	2560 (764)
12−15	12 731 (1283)	9807 (832)	2605 (596)

SD = standard deviation.
Values shown here are not for reaction time corrected isopters and were formed from straight, not curved (spline), lines.

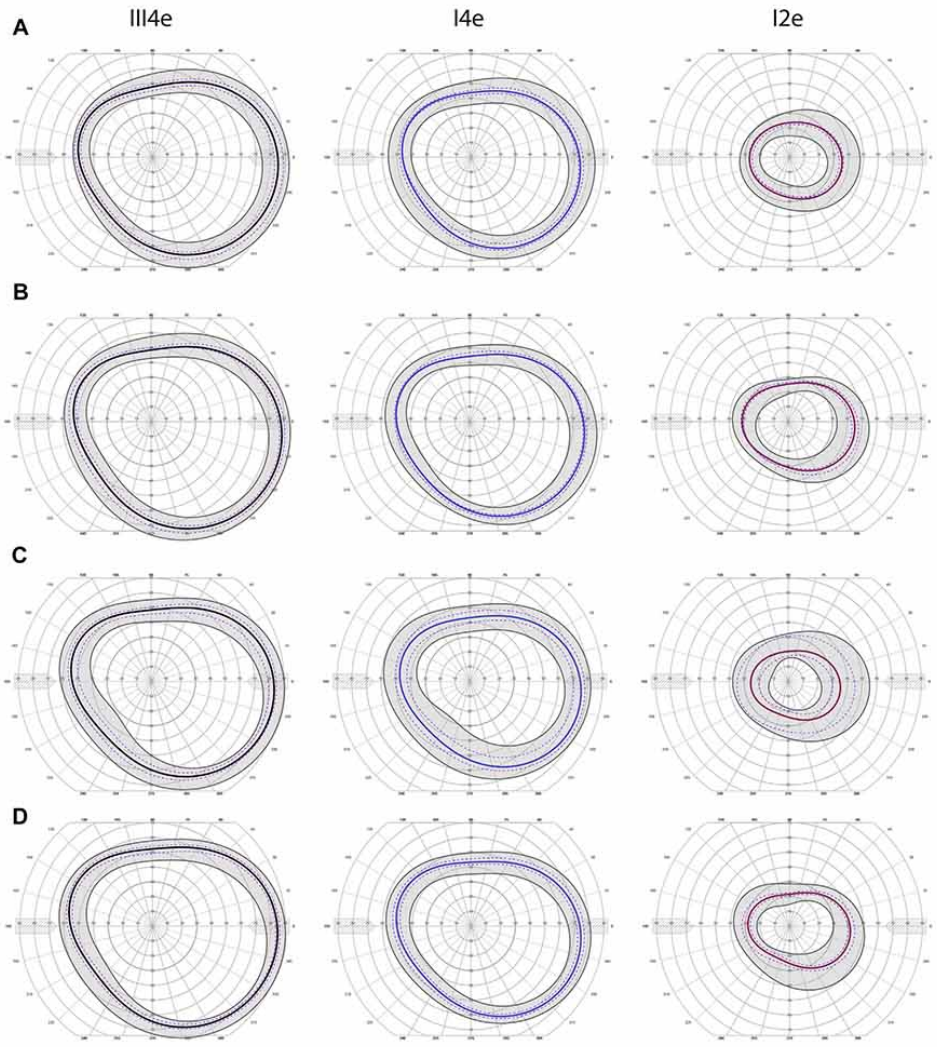

Figure 2. Normative data for kinetic perimetry by age group. **A**, Goldmann isopters representing right eye data for subjects aged 5 to 6 years. **B**, Goldmann isopters representing right eye data for subjects aged 13 to 15 years. **C**, Octopus isopters representing right eye data for subjects aged 7 to 8 years. **D**, Octopus isopters representing right eye data for subjects aged 13 to 15 years. *The central, thick band shows median values, with the dashed (purple) lines encompassing the central 50% of data (interquartile range). The grey, hashed region delineates the area containing 95% of the data. Because fewer young children were able to complete Octopus perimetry to a "good quality" rating, the "lqmm" regression model was not sufficiently robust to use in the youngest group. Thus, children aged 7 to 8 years are shown in **C**.

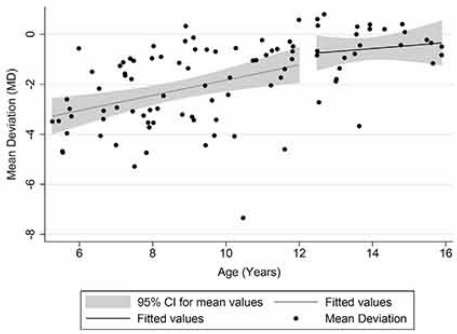

Figure 3. Piecewise linear regression of Humphrey mean deviation (MD) scores with age. CI = confidence interval.

years. For Octopus isopters coefficients of 184.4 (III4e; 95% CI, 98.9−269.8), 129.1 (I4e; 95% CI, 39.6−218.5), and 26.7 (I2e; 95% CI, −40.9 to 94.4) were found. With each perimeter, there was a significant increase in VF area with age with all isopters, except the Octopus I2e. Table 2 lists mean isopter area, by age group for the 3 isopters tested using Octopus perimetry. These values are generated by the Octopus during isopter formation and provide clinically comparable data.

Further analysis was undertaken to generate age-group appropriate normative values, presented on a VF plot, thus enabling clinical interpretation. Figure 2A−D shows these data for isopters III4e (black), I4e (blue) and I2e (red). Figure 2 demonstrates differences in VF area by age for Octopus and Goldmann perimetry, with greatest change in the temporal and inferotemporal field (Appendix 4, available at www.aaojournal.org). Isopter III4e demonstrates a "ceiling effect" when reaching the limit of the Goldmann perimeters' testing area. The inner 2.5% quantile line shifts toward a more eccentric position with age for all isopters on both perimeters, and there is a slight narrowing of the 95% region in older subjects, indicating reduced variability in responses with increasing age.

Mean blind spot area for Goldmann perimetry was $80.6^{\circ 2}$ (SD = 27.7) and $63.5^{\circ 2}$ (SD = 29.2) for Octopus perimetry. No relationship between blind spot size and age was found for either perimeter (Goldmann [$P = 0.75$] or Octopus [$P = 0.07$]).

Static Perimetry

Analysis of MD (a summary statistic produced by the Humphrey perimeter) gives information regarding central VF sensitivity.

Table 3. Average Mean Deviation (MD) Values by Age Group (Humphrey SITA 24-2 FAST)

Age (y)	Average MD Value (SD)
5−6	−3.22 (1.16)
7−8	−2.15 (1.42)
9−11	−1.85 (1.75)
12−15	−0.58 (1.05)

SD = standard deviation.

Regression models revealed an association between age and MD, and further analysis (by piecewise regression; Fig 3) establishes a point of change in this relationship at 12 years of age. Between the ages of 5 and 12 years, the estimated slope is 0.30 (i.e., a 0.3-dB increase in sensitivity per unit increase in age; 95% CI, 0.21−0.40). After 12 years of age, there is no association ($P = 0.526$) and MD values are similar to adult levels (i.e., average MD ≈ 0; Table 3).

Discussion

We report the first normative data for children using common VF tests, using protocols suitable for use in clinical practice. They provide baseline values against which clinical VF tests can be assessed (templates available on request from the authors). Our findings show that the size/area and sensitivity of normal VFs increases with age. We also report new analytical methods for the analysis of kinetic fields (Appendix 1, available at www.aaojournal.org).

Our findings show that with Goldmann perimetry, the mean isopter area for isopter III4e was 17.8% larger, isopter I4e was 11.2% larger, and isopter I2e was 63.1% larger in 15-year-olds compared with 5-year-olds, a large change in VF areas over this 10-year range. This translates into a visible change in isopter appearance between the youngest and oldest subjects (Fig 2A, B), but with overlapping confidence estimates between age groups. It is critical to note that the inner 2.5% quantile line increases in size with age. Thus, previously "normal" values in young children are no longer "normal" as age advances. Most of the developmental change occurs in the temporal and inferotemporal field, with a small increase in nasal field size (Appendix 5, available at www.aaojournal.org).

Direct comparisons of VF area between Goldmann and Octopus perimeters are not appropriate, because the Octopus perimeter has a slightly smaller test area (affecting only far peripheral stimuli) and does not have a "void" area at 90° and 180°.

Humphrey MD values are a commonly used metric in the summary of VF data in children. This study reports normative SITA FAST values in children. Our findings show MD values to be age dependent and their interpretation should therefore account for subject age. Children <10 years of age should not be expected to attain adult VF sensitivity levels (Table 3). Between 10 and 12 years, there is a good likelihood of achieving adultlike results (MD > −2 dB) and children >12 years should be expected to achieve adult sensitivity levels routinely. Likewise, frequency doubling (static) perimetry (FDT) uses an underlying adult normative database, against which test results are compared and children do not reach adult levels of sensitivity with FDT until 14 years of age.[9]

Finally, perimeter-specific assessment factors should be considered when interpreting findings, that is, the ease of positioning child subjects, the effect of audible stimulus presentation, and fatigue effects.

To our knowledge, our study is the largest of its kind to date in children, and assessed multiple common perimetric tests, using clinically suitable protocols and robust analyses. Potential sources of bias, such as learning and fatigue, were

minimized by randomizing test order. We included children without binocular functions/stereopsis to ensure that the sample reflected the target population for VF testing in a clinical setting and evidence has shown that "fellow" eyes in children with strabismus have normal VFs.[11,12]

The study was designed with an awareness of the issues surrounding data capture of subjective responses in children. Our pragmatic approach allowed us to generate normative data for 3 perimetric assessments, but meant we were unable to measure both eyes or assess repeatability in a single sitting. Other limitations include the reduction of sample size after the exclusion of tests that were not rated as having "good" reliability (approximately one-third of the total sample for Octopus and Humphrey perimetry), precluding analysis of Octopus perimetry using the quantile regression model in the 5- to 6-year age group.

It is difficult to compare directly our kinetic data with the extant literature reporting VF size in children, because prior research involved assessments along fewer meridians, using large stimuli (V4e) only,[5,6] or had a small sample and analyzed with parametric methods.[20] However, visual inspection does show that our results in the oldest children are similar to the results of Egge[1] in 14- to 15-year-olds (n = 68, Goldmann perimetry), albeit with a slightly smaller nasal field in our study, but similar confidence estimates.

For Octopus perimetry, normative isopters have been modeled previously in adults using parametric methods and are therefore not comparable with the data presented here. We have produced area data for Octopus perimetry, and elected not to correct for reaction time as children can demonstrate variable reaction times through the course of a single test, and thus our results are not comparable with others.[7] Spline models describe changes of isopter values in relation to isopter area by fitting a nonparametric smooth function using curved lines. The use of linear models in our study, using straight as opposed to curved lines when estimating isopter area, affects the generalizability of these results.

Our findings provide normative, age-dependent VF values in children, to serve as the basis for interpretation of VF test results in children with ophthalmic disease. They provide a means of bridging the gap in normative data for Goldmann,[1,3] Octopus,[4] and Humphrey[2] perimetry. We provide evidence for linear VF growth during childhood (between 5 and 15 years) as measured with kinetic perimetry (both Goldmann and Octopus), whereas static perimetry (Humphrey SITA) results reach adult levels at 12 years of age. We suggest that interpretation of perimetric findings should be based on knowledge of the normal range of area/size or sensitivity reported here. For example, when monitoring progressive VF loss longitudinally in young children, a failure to demonstrate larger/more sensitive VFs over a number of years may indicate loss of VF function or arrested development, rather than stability. Further planned work in this program of research will assess the utility of perimetry in children with glaucoma and neuro-ophthalmic disease, developing the understanding of the role of perimetry in diagnosing and monitoring ophthalmic disease in children.

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[1] Life Course Epidemiology and Biostatistics Section, University College London Institute of Child Health, London, UK.

[2] Ulverscroft Vision Research Group, London, UK.

[3] Moorfields Eye Hospital NHS Foundation Trust, London, UK.

[4] Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK.

[5] University College London Institute of Ophthalmology, London, UK.

[6] Clinical Epidemiology, Nutrition and Biostatistics Section, University College London Institute of Child Health, London, UK.

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*Jugnoo S. Rahi leads the OPTIC Study Group.

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Author Contributions:

Conception and design: Patel, Cumberland, Walters, Russell-Eggitt, Rahi

Analysis and interpretation: Patel, Cumberland, Walters, Russell-Eggitt, Cortina-Borja, Rahi

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Abbreviations and Acronyms:
D = diopter; **MD = mean deviation; **RE** = refractive error; **SITA** = Swedish Interactive Thresholding Algorithm; **VF** = visual field.

Correspondence:
Jugnoo S. Rahi, PhD, FRCOphth, UCL Institute of Child Health, 30 Guilford Street, London, WC1N 1EH, UK. E-mail: j.rahi@ucl.ac.uk.

Modeling normative kinetic perimetry isopters using mixed-effects quantile regression

Dipesh E. Patel
Life Course Epidemiology and Biostatistics Section, University College London Institute of Child Health, London, UK
Ulverscroft Vision Research Group, London, UK
Moorfields Eye Hospital National Health Service Foundation Trust, London, UK
Great Ormond Street Hospital for Children National Health Service Foundation Trust, London, UK

Marco Geraci
Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA

Mario Cortina-Borja
Clinical Epidemiology, Nutrition and Biostatistics Section, University College of London Institute of Child Health, London, UK

Kinetic perimetry is used to quantify visual field size/sensitivity. Clinically, perimetry can be used to diagnose and monitor ophthalmic and neuro-ophthalmic disease. Normative data are integral to the interpretation of these findings. However, there are few computational developments that allow clinicians to collect and analyze normative data from kinetic perimeters. In this article we describe an approach to fitting kinetic responses using linear quantile mixed models. Analogously to traditional linear mixed-effects models for the mean, linear quantile mixed models account for repeated measurements taken from the same individual, but differently from linear mixed-effects models, they are more flexible as they require weaker distributional assumptions and allow for quantile-specific inference. Our approach improves on parametric alternatives based on normal assumptions. We introduce the R package `kineticF`, a freely available and open-access resource for the analysis of perimetry data. Our proposed approach can be used to analyze normative data from further studies.

Introduction

Sensitivity to light reduces with increasing eccentricity from the center of the visual field. Kinetic perimetry assesses the location at which moving light of a fixed size/intensity can be seen and is used to quantify visual field sensitivity. The location of each test point is recorded as a polar coordinate, and points are joined to form an isopter, denoting a line of differential light sensitivity, within which light of a particular size/intensity can be perceived.

Constructing robust normative perimetry standards provides an evidence base for interpretation of clinical/research findings—aiding detection of visual field defects. Analysis of normative kinetic perimetry data requires an understanding of anatomical and physiological characteristics, and the correct application of appropriate statistical methods. However, the analytical methods currently employed in the literature do not take into account the repeated-measures structure of a kinetic isopter, nor do they adequately address the lack of normality in the empirical distribution of data points.

Niederhauser and Mojon (2002) summarized kinetic isopters at each meridian with the mean and 95% confidence intervals. Similar methods have been used by other researchers (Egge, 1984; Wilscher, Wabbels, and Lorenz, 2010) though they assume symmetric distributions along test meridians. There are two issues

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with this approach: It can define poorly fitted regions of uncertainty that may fall outside the edge of the perimeter test surface or cause crossing of confidence bands; also, as it is not model-based, it cannot be used for inferential purposes (e.g., to compare goodness-of-fit or to determine whether the resulting normative curves and confidence regions need further adjustment by relevant covariates, such as age). Other techniques for summarizing normative fields, such as total isopter area (Bjerre, Codina, & Griffiths, 2014; Quinn, Fea, & Minguini, 1991) and visual field extent along meridians (Wilson, Quinn, Dobson, & Breton, 1991) do not provide reference values that are easily interpretable in a clinical setting.

Isopter data may show conditional distributions that do not conform to normality assumptions, such as symmetry and constant variance (homoscedasticity), either on the observed or the transformed (e.g., logarithmic) scale of the outcome. For these reasons, modeling based on mean (normal) regression can lead to incorrect inference. Even when approximate normality is achieved after transformation, back-transformation of conditional expectations is troublesome as it may lead to estimates and/or confidence regions outside the admissible range of the outcome. Moreover, isopter data that are collected repeatedly on the same subject are correlated by design. While mixed-effects models for the mean account for the clustered design, they are still subject to strong distributional assumptions and back-transformation issues.

As an alternative to mean regression, we consider quantile regression (QR; Koenker, 2005), which introduces weak assumptions on the distribution of the error and therefore is robust to deviations from normality. For this reason, no transformation is required—note, however, that even when transformations are introduced to achieve linearity, back-transforming quantiles is a simple task (see for example, Geraci & Jones, 2015). More specifically, in this article we address the analytical challenges of modeling isopter data using mixed-effects models for conditional quantiles called linear quantile mixed models (LQMMs; Geraci & Bottai, 2014). The inclusion of subject-specific effects in mixed-effects models allows for within-subjects correlation resulting from repeated measurements. This approach yields clinically appropriate estimates within expected clinical ranges and correct inference from kinetic perimetry data.

Here we report the application of LQMMs to normative kinetic isopter data obtained from healthy children (Patel, Cumberland, Walters, Russell-Eggitt, Cortina-Borja et al., 2015) using the R (The R project for Statistical Computing, version 3.1.2; R Core Team, 2016) package `kineticF` (Patel & Cortina-Borja, 2015). The `kineticF` package is a collection of functions for cleaning, processing, visualization, and analysis of manual (Goldmann) and automated (Octopus 900) kinetic visual field data, which depends on the package `lqmm` (Geraci, 2014) used to fit QR models with random effects.

Methods

Data

The data used in the examples here were collected at Moorfields Eye Hospital, London, as part of a wider program of research, which has been described elsewhere (Patel, Cumberland, Walters, Russell-Eggitt, & Rahi, 2015). Briefly, we recruited children without an ophthalmic condition that affects the visual field to generate normative data and explore visual field development in childhood. Informed written consent was obtained from the children's parents/guardians. This study was approved by the National Health Service Research Ethics Committee for London–Bloomsbury and conforms to the tenets of the Declaration of Helsinki.

Children aged 5 to 15 years were examined by one clinician (DEP) under clinical conditions using Goldmann and Octopus kinetic perimeters (Haag-Streit, Bern, Switzerland). Manual Goldmann data were scanned and digitized using Engauge digitizer software (open-source, www.digitizer.sourceforge.net). Octopus data were extracted from the perimeter and processed using the R package `kineticF` (Patel & Cortina-Borja, 2015) available from the Comprehensive R Archive Network repository.

Statistical methods

Data were collected in polar coordinates (r, θ) defining points along meridians. Due to the cyclical nature of the isopters (Figure 1A), we used harmonic linear predictors in our regression models. For these data, a simple model with sine and cosine terms of periods π and $\pi/2$ could be specified as follows:

$$r = \beta_0 + \beta_1\cos(\theta) + \beta_2\sin(\theta) + \beta_3\cos(2\theta) + \beta_4\sin(2\theta) + \varepsilon, \quad (1)$$

where r is the isopter value corresponding to meridian θ and the βs are the model's parameters. Of course, Model 1 can include interactions between the sine and cosine terms, or higher frequency harmonics, and be adjusted for confounders such as age and sex. Typically, the error term ε is assumed to be normal, with zero mean and constant variance.

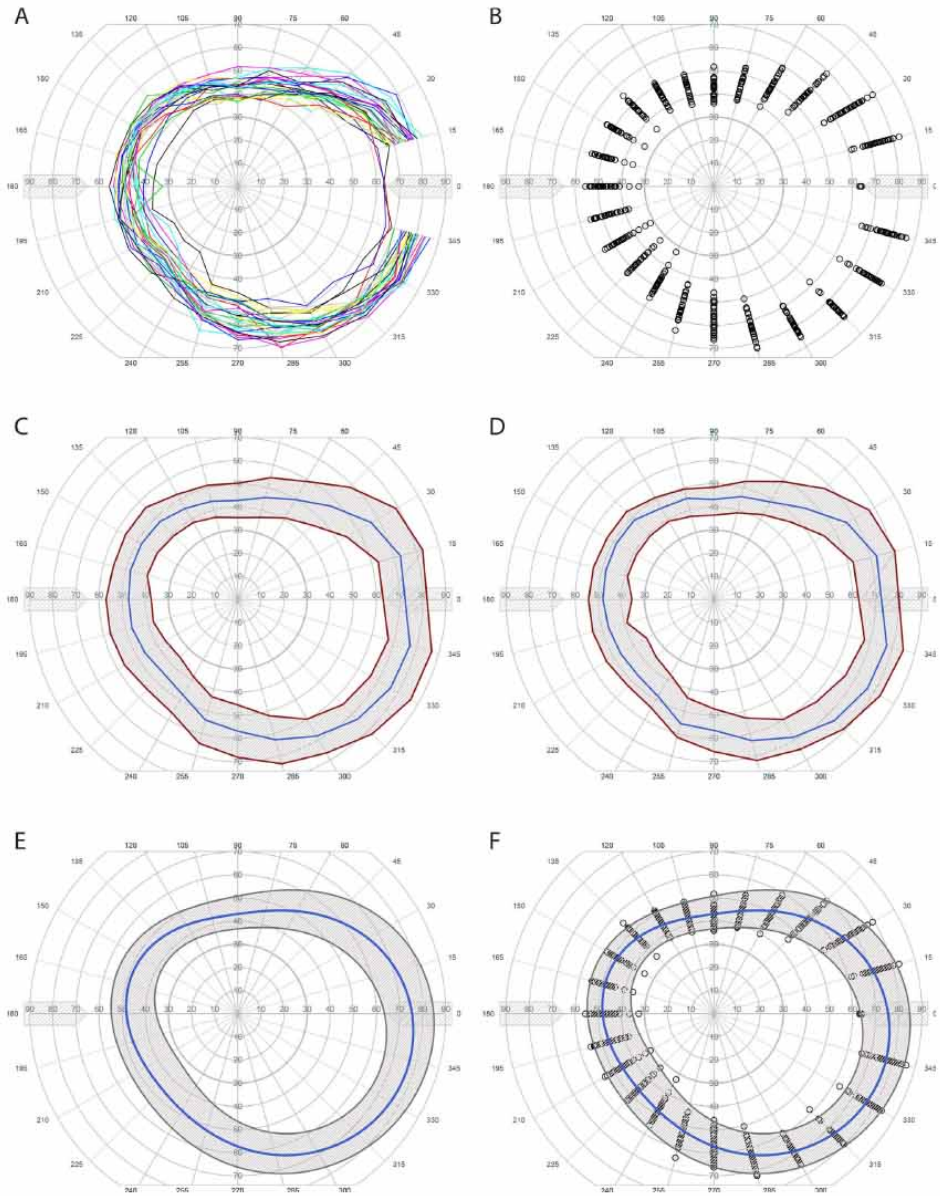

Figure 1. Subject lines (A), points (B), and methods of summarizing normative data; mean and 95% confidence interval (C), mean with 2.5% and 97.5% quantiles (D), and a linear quantile mixed-effects model without (E) and with (F) subject data points.

Since the goal is to produce normative standards (i.e., reference charts), we need to predict specific isopter quantiles. Under normal assumptions, the $100 \cdot p$th centile of the conditional distribution of r from Equation 1 is defined as

$$Q_r(p) = \beta_{0,p} + \beta_1 \cos(\theta) + \beta_2 \sin(\theta) + \beta_3 \cos(2\theta) + \beta_4 \sin(2\theta), \quad (2)$$

where $\beta_{0,p}$ is an intercept that depends on the quantile p. However, note that the slopes in Equation 2 are constrained by the normal model to be the same for all quantiles. This means that all the individuals in the sample are assumed to have the same distribution, except for a shift $\beta_{0,p}$, which is determined by the normal distribution.

In QR, individual conditional distributions are allowed to differ from subject to subject by letting all the parameters, including the slopes, vary with p. Thus, the location, scale, and shape of the error term ε are not determined by a theoretical distribution (e.g., normal) but are modeled empirically.

A QR approach is particularly appropriate to model isopter data. The distribution of points along meridians (as observed from multiple subjects) is skewed and leptokurtotic (Figure 1B). Rather than use a transformation (e.g., logarithmic) of these values to achieve normality, we used QR models, which do not require specific distributional assumptions on the error (distribution-free), adequately describe skewed and kurtotic distributions, and operate on the data's original scale. In these models, we define the regression parameters in relation to a set of quantile levels, namely 2.5%, 50%, and 97.5%, which describe the central tendency and the central 95% of the conditional distribution. Moreover, since by design the isopter data are clustered within individuals, we used LQMMs as proposed by Geraci and Bottai (2014) to account for the within-subjects correlation. For our data, we considered several specifications of LQMMs.

In our model selection strategy, we first used a forward stepwise approach in which terms were included if their parameter estimates reached a 10% significance level. We only considered random effects terms on the intercept of each model given that, for all models fitted, adding other random effects in the models did not improve the trade-off between goodness-of-fit and number of parameters as measured with the Bayesian Information Criterion (Kuha, 2004).

The final LQMM

$$Q_r(p) = (\beta_{0,p} + b_{0,p}) + \beta_{1,p} \cos(\theta) + \beta_{2,p} \sin(\theta) + \beta_{3,p} \cos(2\theta) + \beta_{4,p} \sin(2\theta) + \beta_{5,p} \sin(\theta) \times \cos(2\theta), \quad (3)$$

included a random intercept ($b_{0,p}$) and a fixed effect for the interaction between cosine and sine terms ($\beta_{5,p}$), along with fixed effects for individual cosine and sine terms. Note that all regression coefficients depend on the particular centile p.

The R package `kineticF` makes use of the routines from the package `lqmm` (Geraci, 2014) to fit QR models with random effects. The output from `lqmm` is subsequently taken by `kineticF` to provide graphical and statistical summaries matching those produced by common perimeters, thus immediately facilitating clinical interpretation. Cubic smoothing spline models were used to smooth the predicted isopters between consecutive meridians by interpolating the fitted quantile values in each meridian. The smoothing parameter of these spline models was chosen using a cross-validation procedure (Green & Silverman, 1994). This interpolating process is included in `kineticF` and produces smooth bands for specific quantiles of the isopters. These predicted normative bands avoid assuming a constant standard deviation and symmetry across meridians.

These outputs were then formatted as templates for use in both clinical and research settings (available from http://e-lucid.com/i/video_and_images/optic_templates.html). All data management and statistical modeling was performed using Microsoft Excel 2010® and R.

Results

Data were collected from 154 children. The examples shown here are from 30 subjects aged 8 to 11 years, plotting isopter I4e.

Figure 1A displays the trajectories of individuals, demonstrating the need for modeling the within-subject structure present in the dataset. (Note that the lack of data points along the 0° meridian corresponds to the void [hashed] area within the Goldmann perimeter bowl—that is, an area where no points can be plotted.) Figure 1B shows the sample data points along 24 meridians located at 15° intervals; the asymmetry of these observations along each meridian is apparent. For example, along the 150° meridian, there is a concentration of points at 50° eccentricity (near the limit of the nasal field), with a long lower tail extending to approximately 35°. Figure 1C and D show these data's mean and 95% confidence interval, and the 2.5th, 50th, and 97.5th empirical centiles along each meridian, which are methods that have been used previously in the literature. Finally, Figure 1E and F show the fitted mixed-effects QR model as defined in Equation 3 with predicted and smoothed curves for the 2.5%, 50%, and

97.5% quantiles, without and with observed data points, respectively.

Discussion

We have applied robust statistical methods to the modeling of normative kinetic perimetry data sampled from multiple subjects and developed a collection of visual and analytic software routines to carry out similar analyses. Our approach is robust against deviations from normality and homoscedasticity, and represents a substantial advance to current practice in that it lays the basis for statistical model comparisons based on goodness-of-fit criteria, and improves clinical interpretation by providing smooth quantile curves representing the variability of normative visual fields. Since these two aspects have not been fully addressed in the literature, we cannot compare our approach with other modeling strategies (Vonthein et al., 2007). However, Figure 1F shows a substantial improvement with respect to other approaches that do not use regression models, namely Figure 1C and D. Both are flawed: The former assumes that the mean and a constant dispersion measure are enough to model the conditional distribution; the latter estimates the quantiles of interest for each isopter without reference to the whole data set or to the within-subjects correlation, and does not produce smooth normative bands.

A potential limitation of methods based on QR is that small samples (data sparsity) may lead to erratic estimates of tail quantiles and, in the worst case, to quantile crossing. This can be avoided by ensuring a balanced design and an adequately sized sample.

As noted, we used a cross-validation criterion to determine the smoothness of the cubic splines that interpolated the quantiles of the isopters predicted by our model. This could have been achieved in a Bayesian setting assuming a prior distribution for the smoothing parameters and estimating them with, for instance, the median of its posterior distribution.

Our approach can be applied to clinical data from control subjects thus providing normative data against which observations from case subjects can be compared. Without defining these normative standards, it is impossible to accurately assess disease status. The mixed-effects quantile models described in this paper can be readily applied to perimetric data using packages `lqmm` and `kineticF`, which are freely available from public repositories. Our findings support the use of the models reported here when generating normative kinetic perimetry standards.

Keywords: `kineticF`, *linear quantile mixed models,* `lqmm`, *kinetic perimetry, normative data, OPTIC study*

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Corresponding author: Mario Cortina-Borja.
Email: m.cortina@ucl.ac.uk.
Address: Clinical Epidemiology, Nutrition and Biostatistics Section, UCL Institute of Child Health, London, UK.

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9.8.2 Articles

As part of our patient and public engagement, we were interviewed for Moorfields Infocus magazine.

EYESITE'S DOGTOR WAG

www.eyesite.nhs.uk

Visual fields test
Visual fields tests are an important part of eye care as the results tell eye doctors and optometrists all sorts of useful information about the problems you might be having with your eyes. Here we find out more about them.

What is a visual field?
Your visual field is the area of space you can see up and down and to the sides, without moving your eyes.

Why do children have visual field tests?
Eye problems in children affect the eyesight, but can also affect the visual field. Doing a visual field test helps us measure exactly what people can see.

When was the first visual field test done?
The first ever visual field test was done almost 2,000 years ago! Modern visual field tests date back about 60 years.

Does it involve using special machines?
Yes – testing the visual field usually involves using big, bowl-shaped machines that look like satellite dishes.

Dogtor Wag talks visual field tests with Dipesh Patel

Dipesh Patel is a research assistant/honorary research orthoptist, and part of a team undertaking research into the best ways to carry out a visual fields test in children. Here he tells Dogtor Wag why it's important to find the best visual fields test for children.

Why are you carrying out research into visual field testing?
We are doing our research because we want to find out the best way of testing visual fields in children, which isn't known as most research so far has been on adults.

When did the study start and when will it finish?
We started in January 2012 and will finish at the end of 2015.

Can you describe what happens to children in your research project?
We ask children to take a few different tests, to see which ones they like doing, and to see whether the different tests give the same results. All of the tests involve sitting at a visual field test machine with one eye covered. Little lights flash up in the bowl, and whenever a child sees a light, they press a buzzer. Lots of children say doing the test is like playing a videogame!

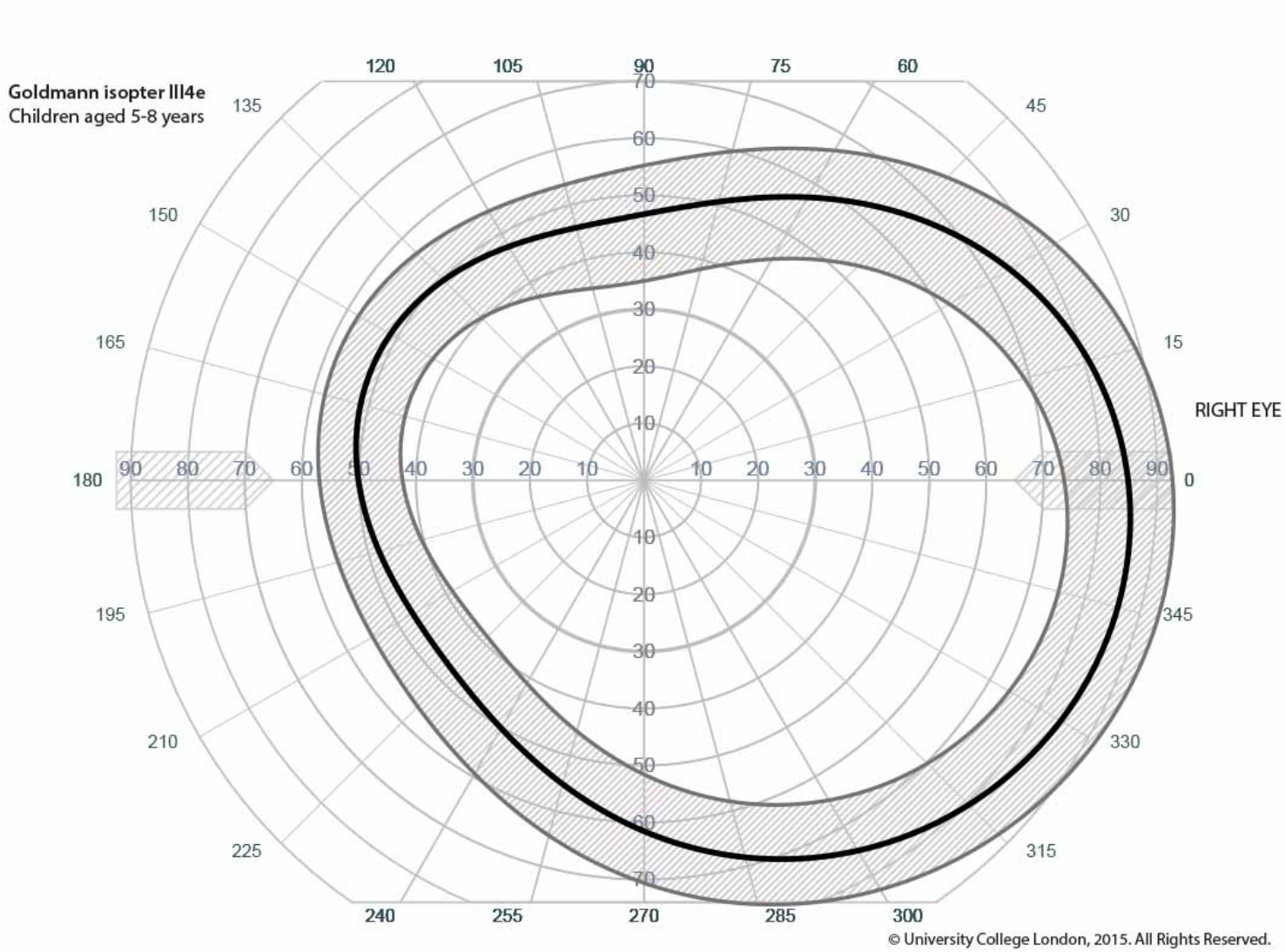
How many children are taking part in your study?
So far, over 200 children have taken part, and we hope to have 50 more take part by the end of the study.

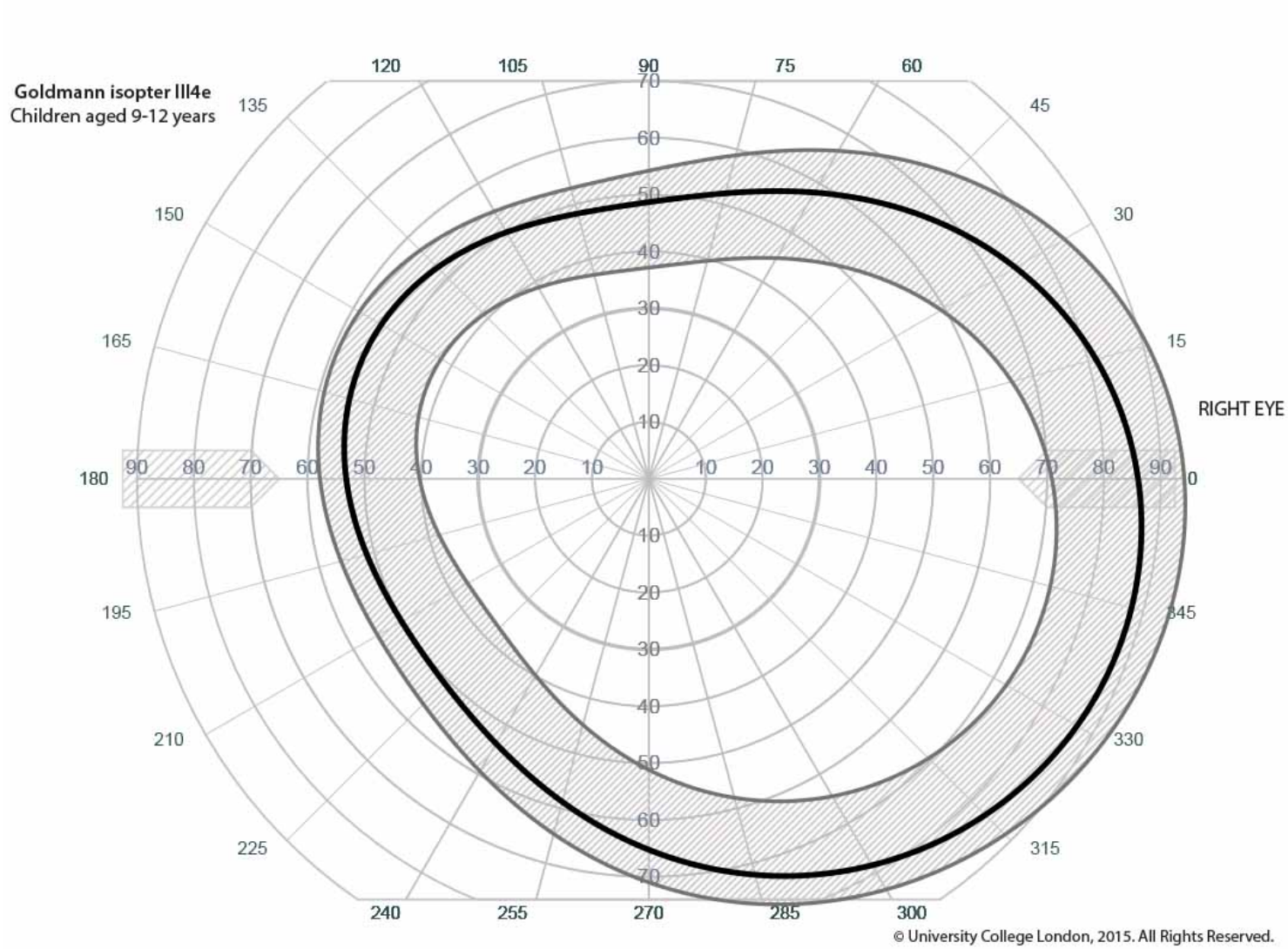
Who will you tell about your research findings?
Our results will help eye doctors make decisions about how to treat eye problems, so we will make sure that the information is available to doctors and other scientists. We also let patients and the public know, partly through Guide Dogs – the charity that is funding us – and the other organisations who are involved, including the NIHR biomedical research centre at Moorfields and the Ulverscroft vision research group.

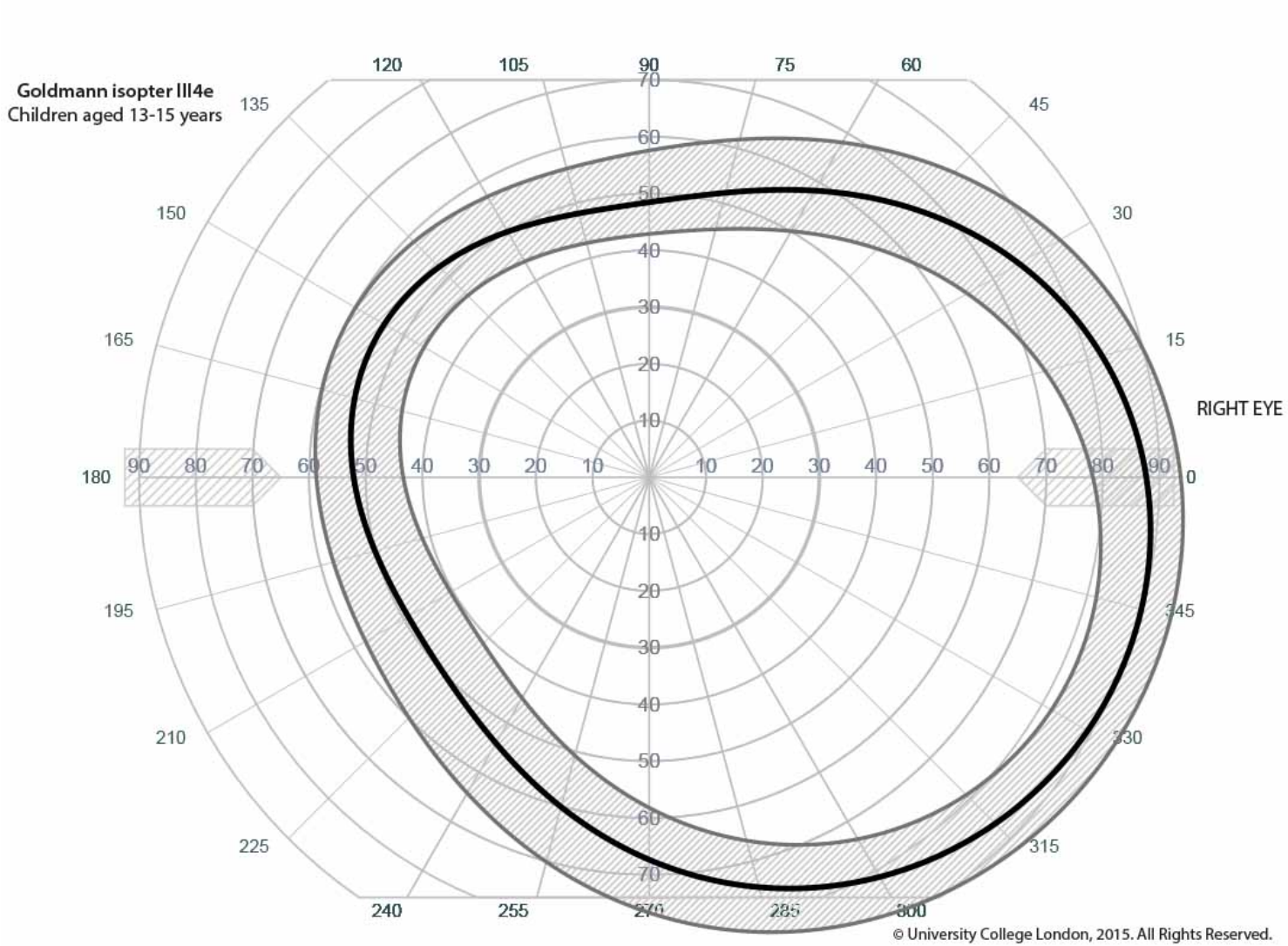
What's the most interesting thing you have found out to date?
So far, we have found that lots of children can take visual field tests and do really well on them, even if they are very young, but some machines are easier to use than others. We've also found that children and young people don't have the same visual fields as adults. This is important for doctors to know when they are looking at visual field test results in children to see if there is a problem.

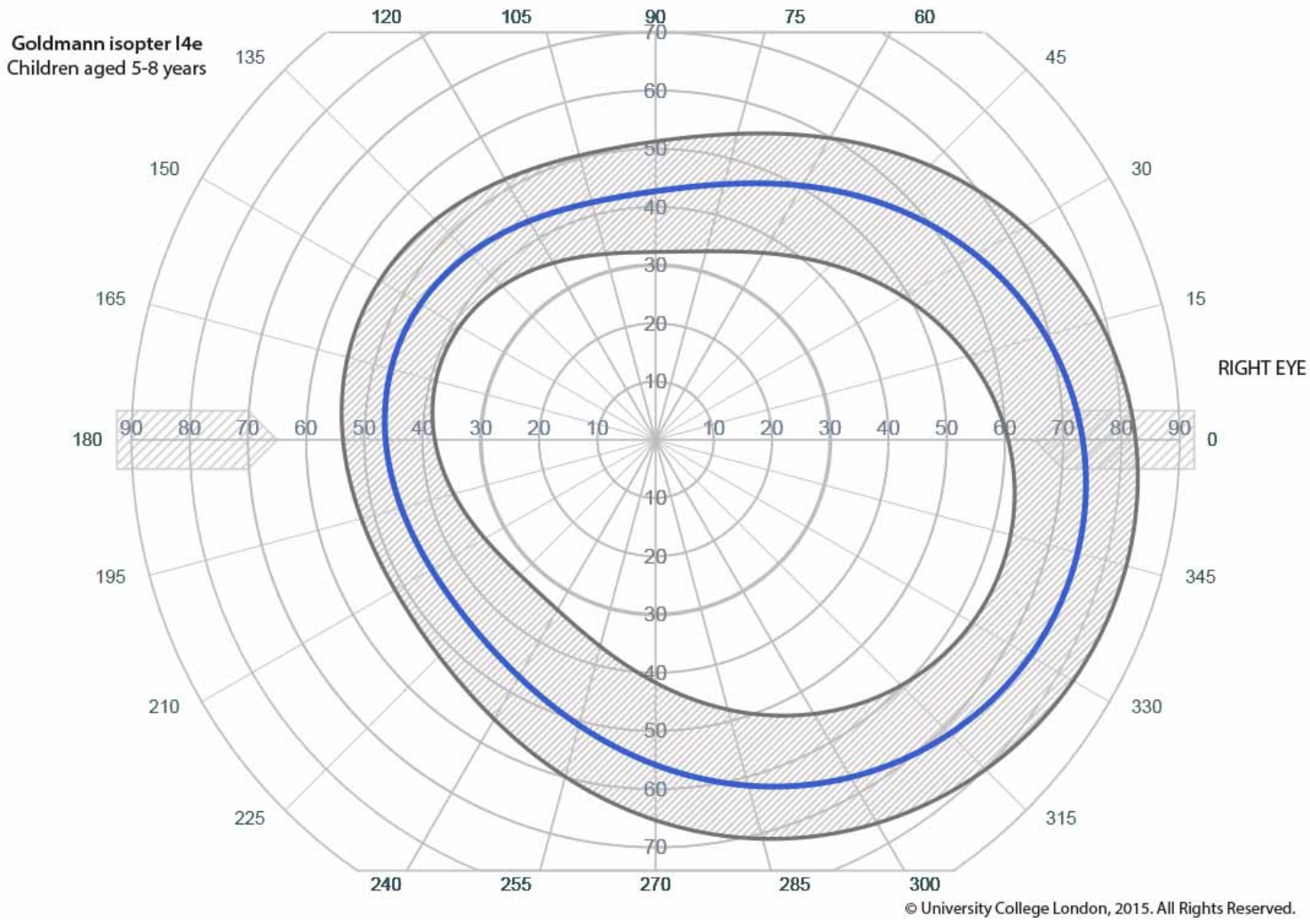
9.8.3 Normative visual field templates

The following templates were published by UCLB (http://e-lucid.com/i/video_and_images/optic_templates.html) from the findings of the OPTIC study. They are designed to be printed as overlays to aid interpretation of kinetic perimetry results in children. Templates are available for isopters III4e, I4e and I2e using Goldmann and Octopus perimeters and are split by age groups; 5-7 years, 8-11 years and 12-15 years. These templates are freely available for use in both routine clinical practice and research.








Goldmann isopter I4e
Children aged 5-8 years
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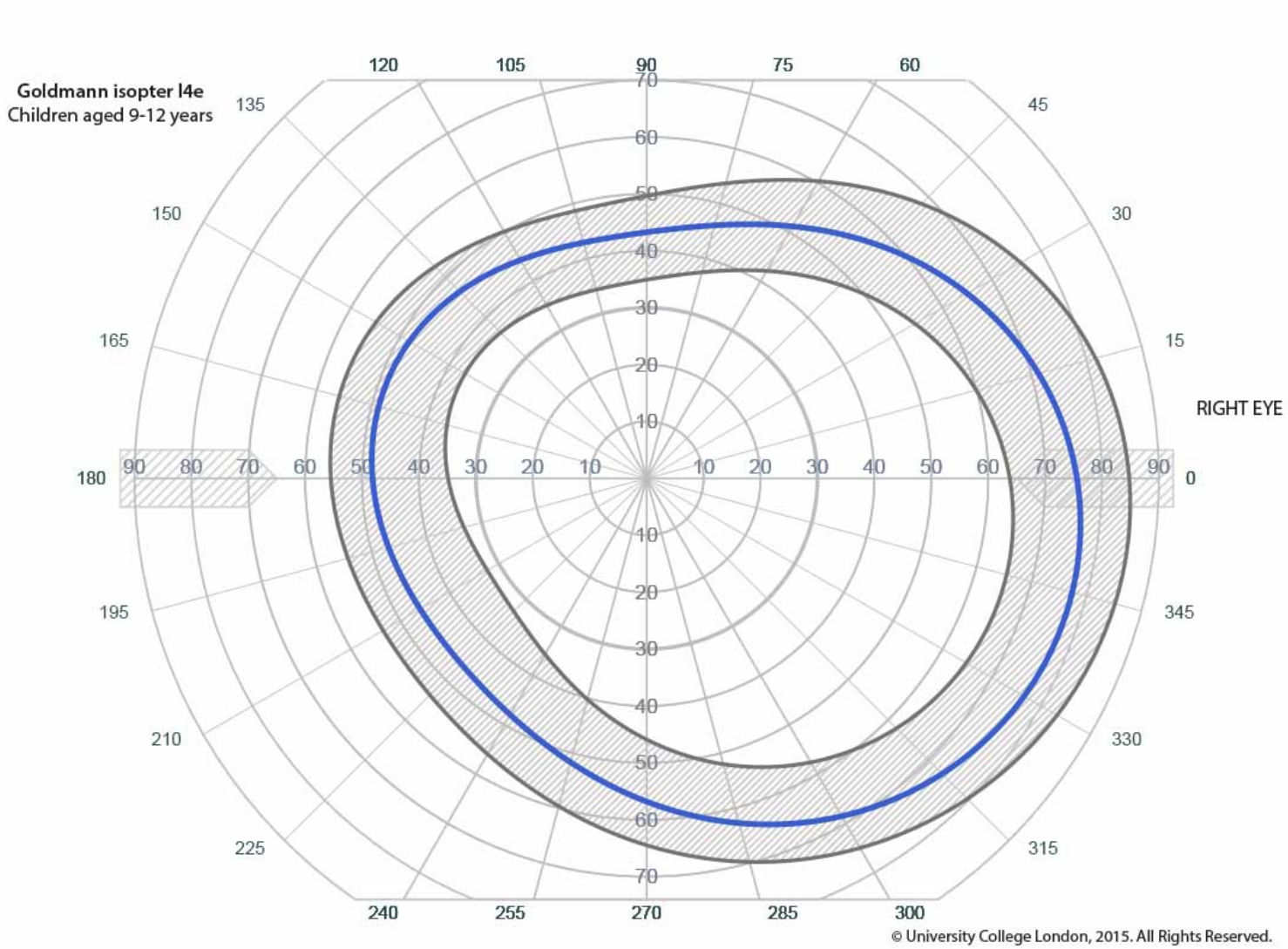

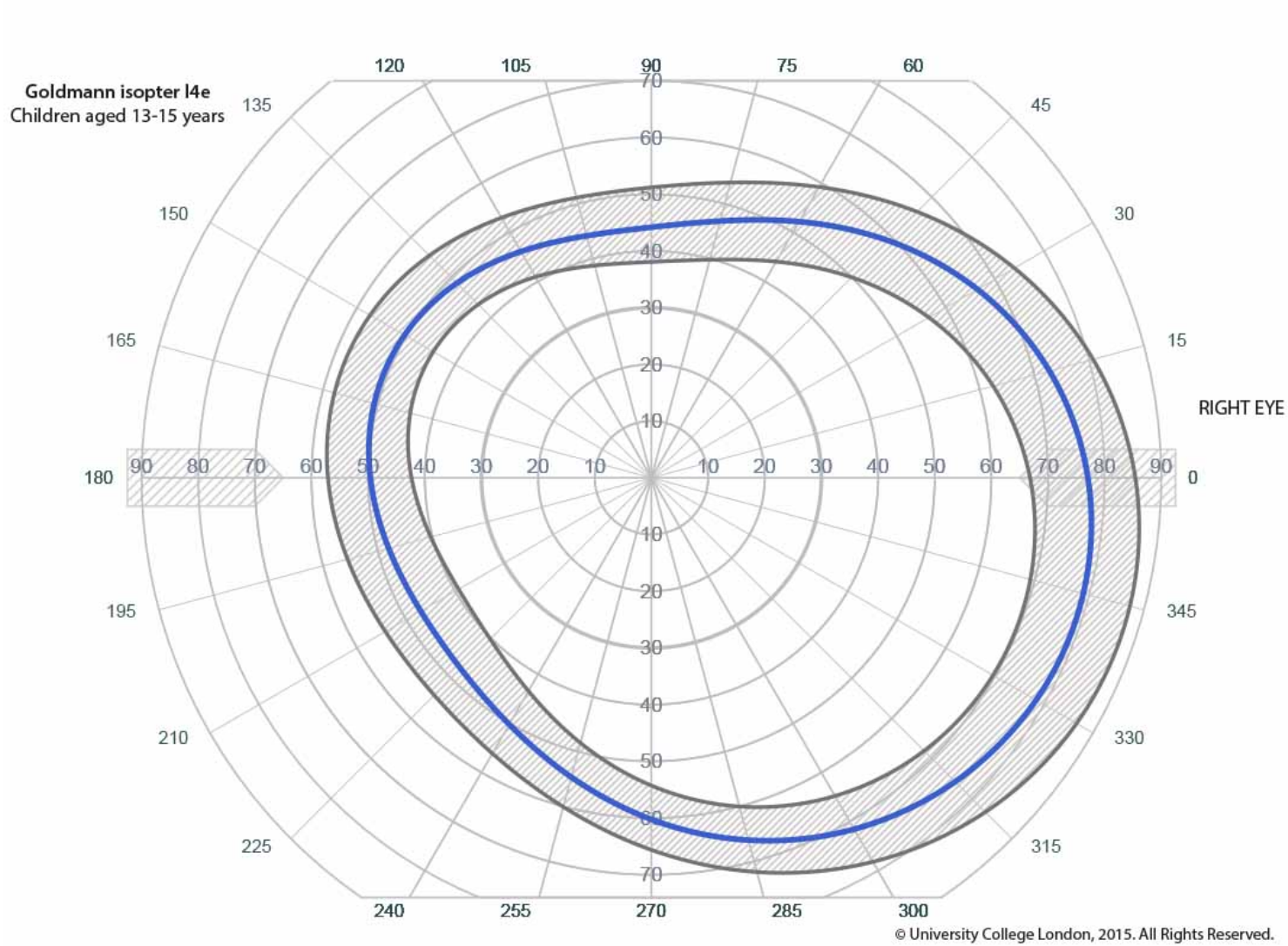

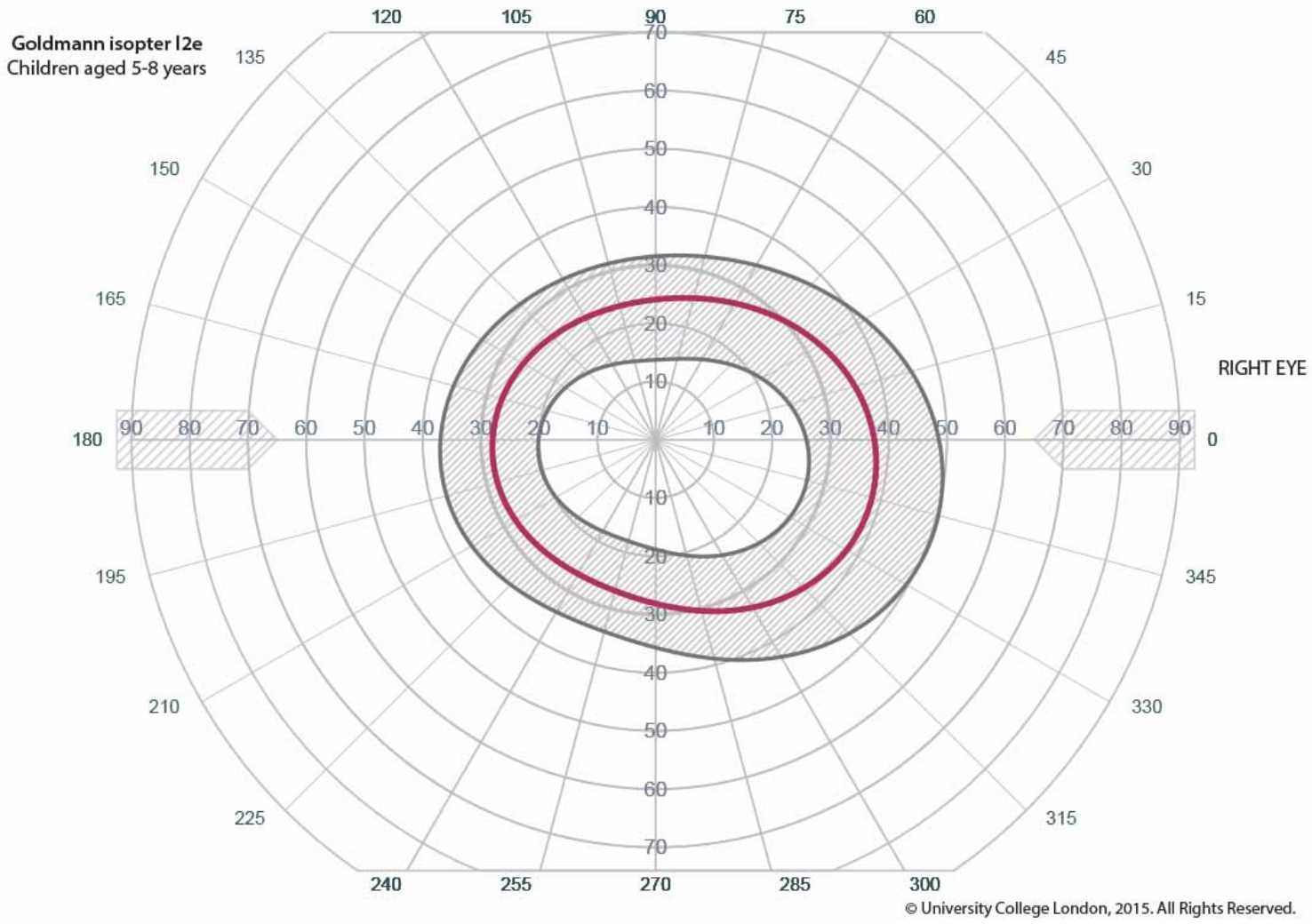

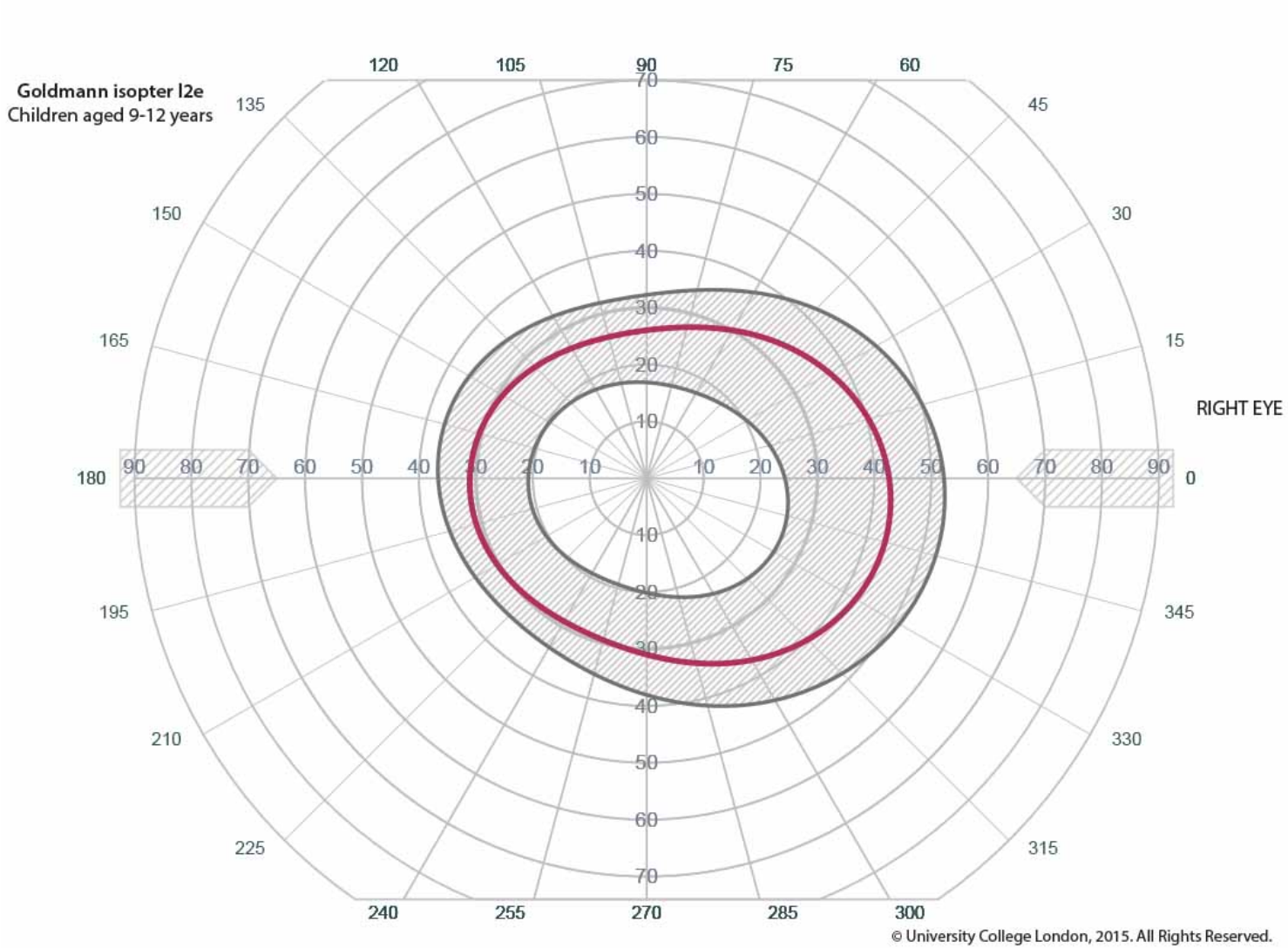

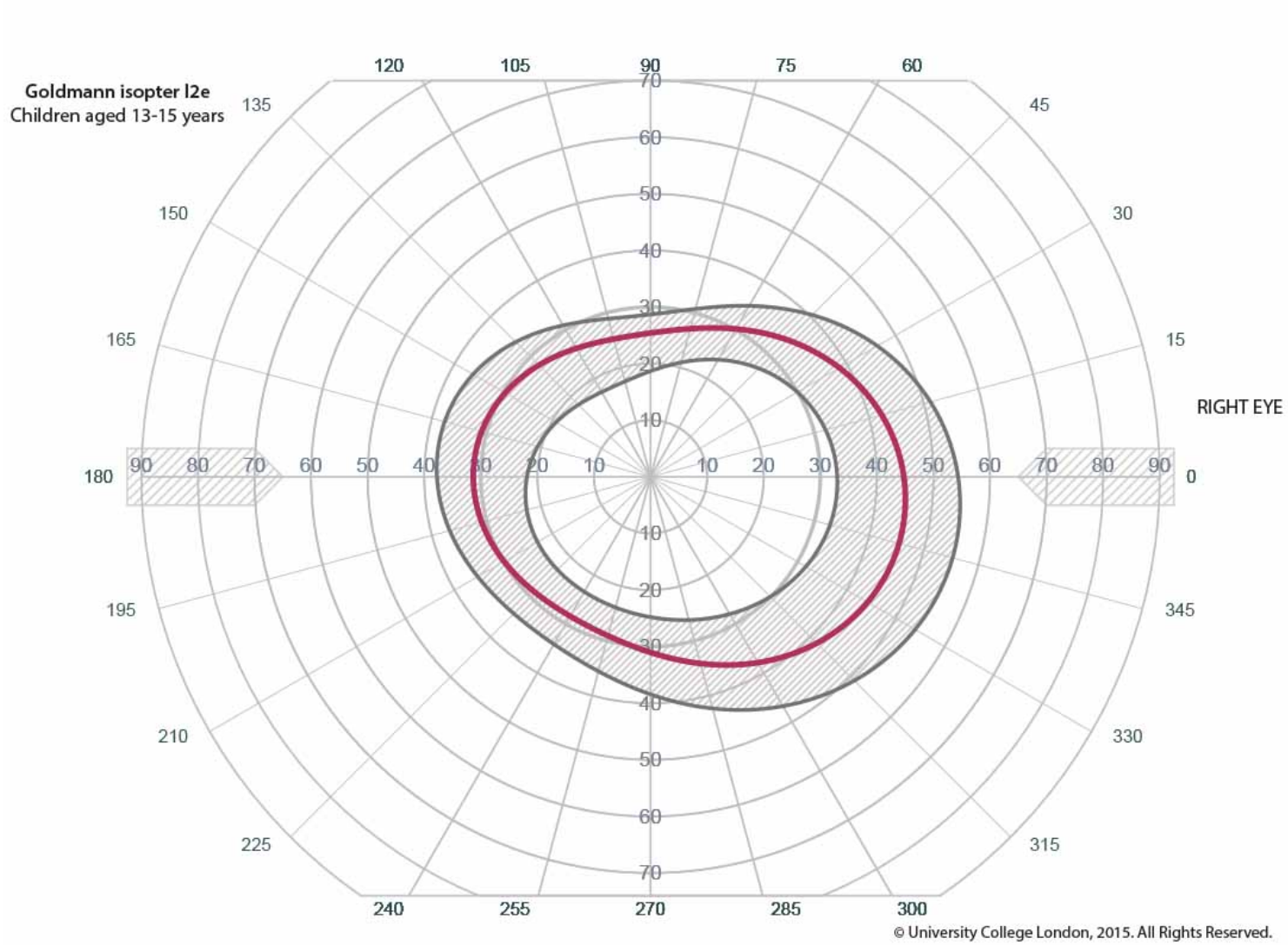
Goldmann isopter I2e
Children aged 13-15 years
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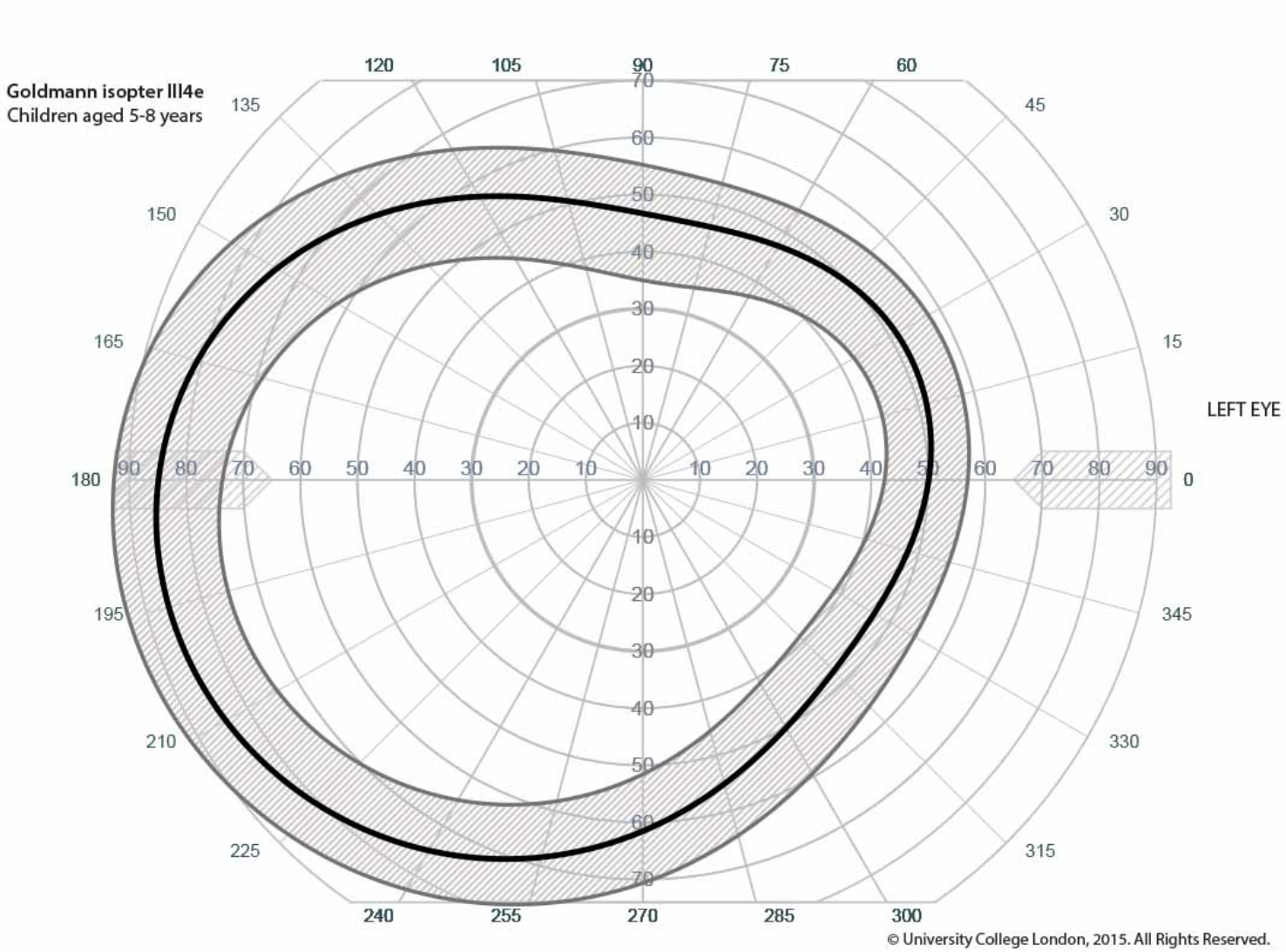

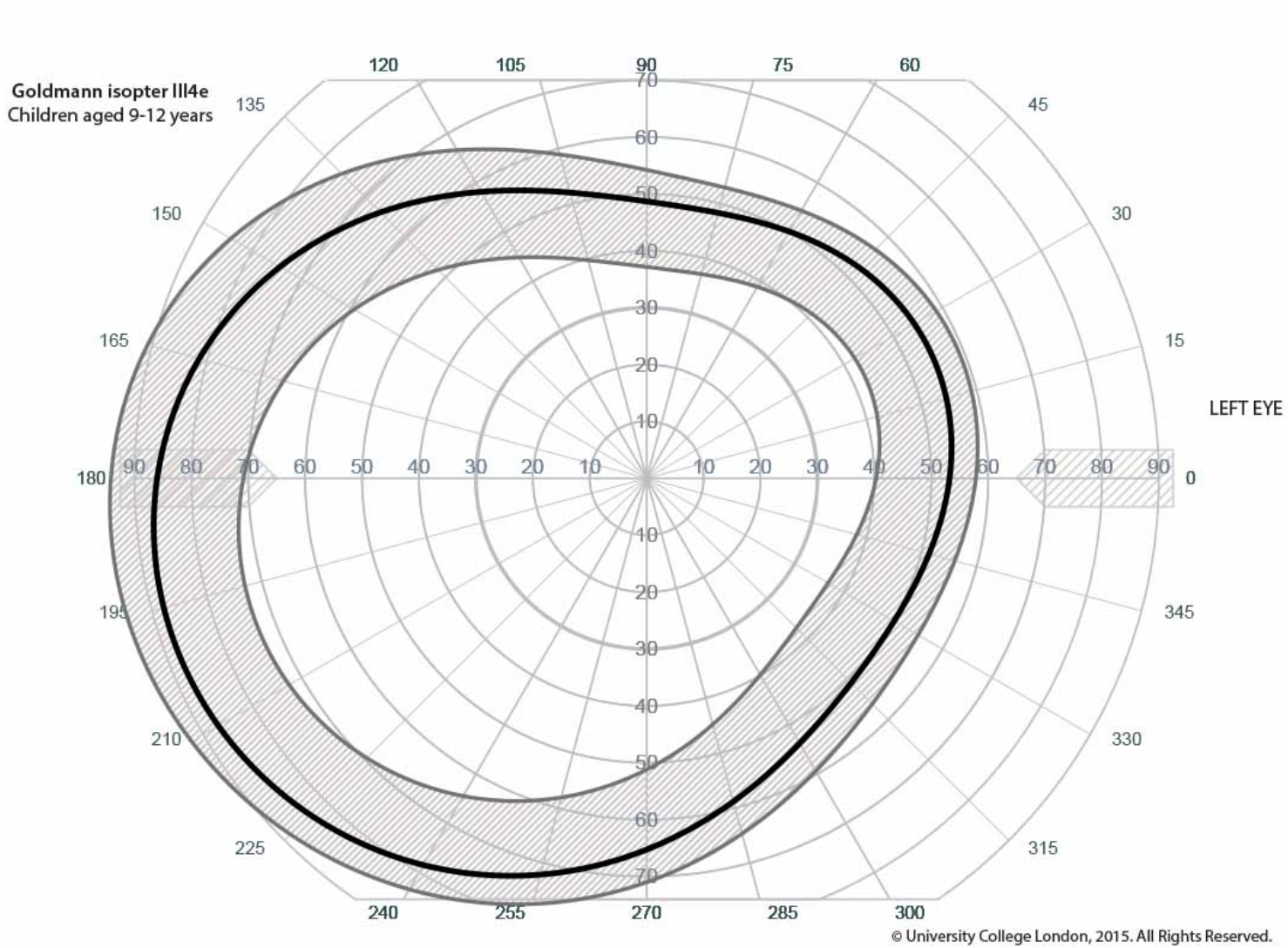

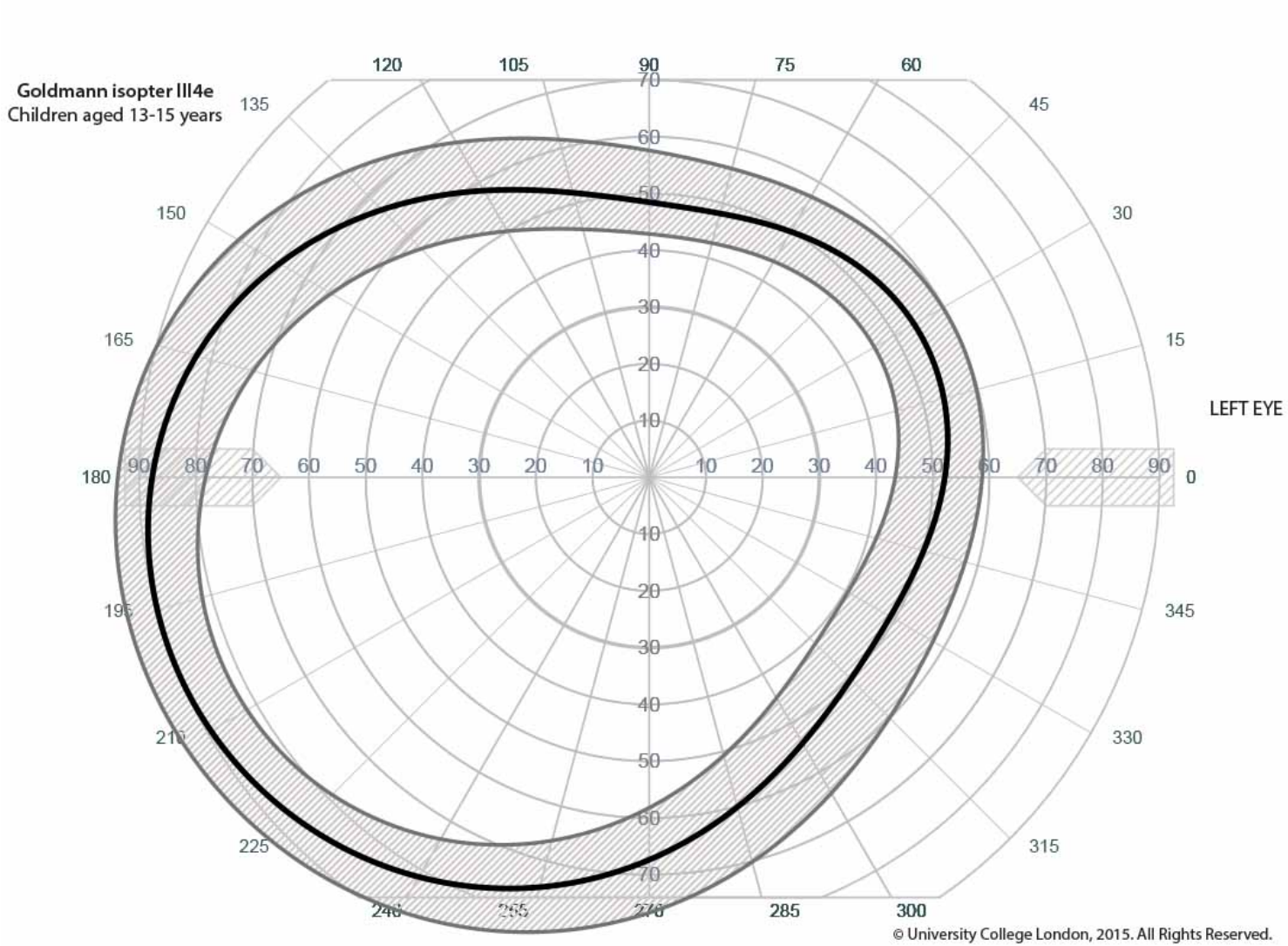

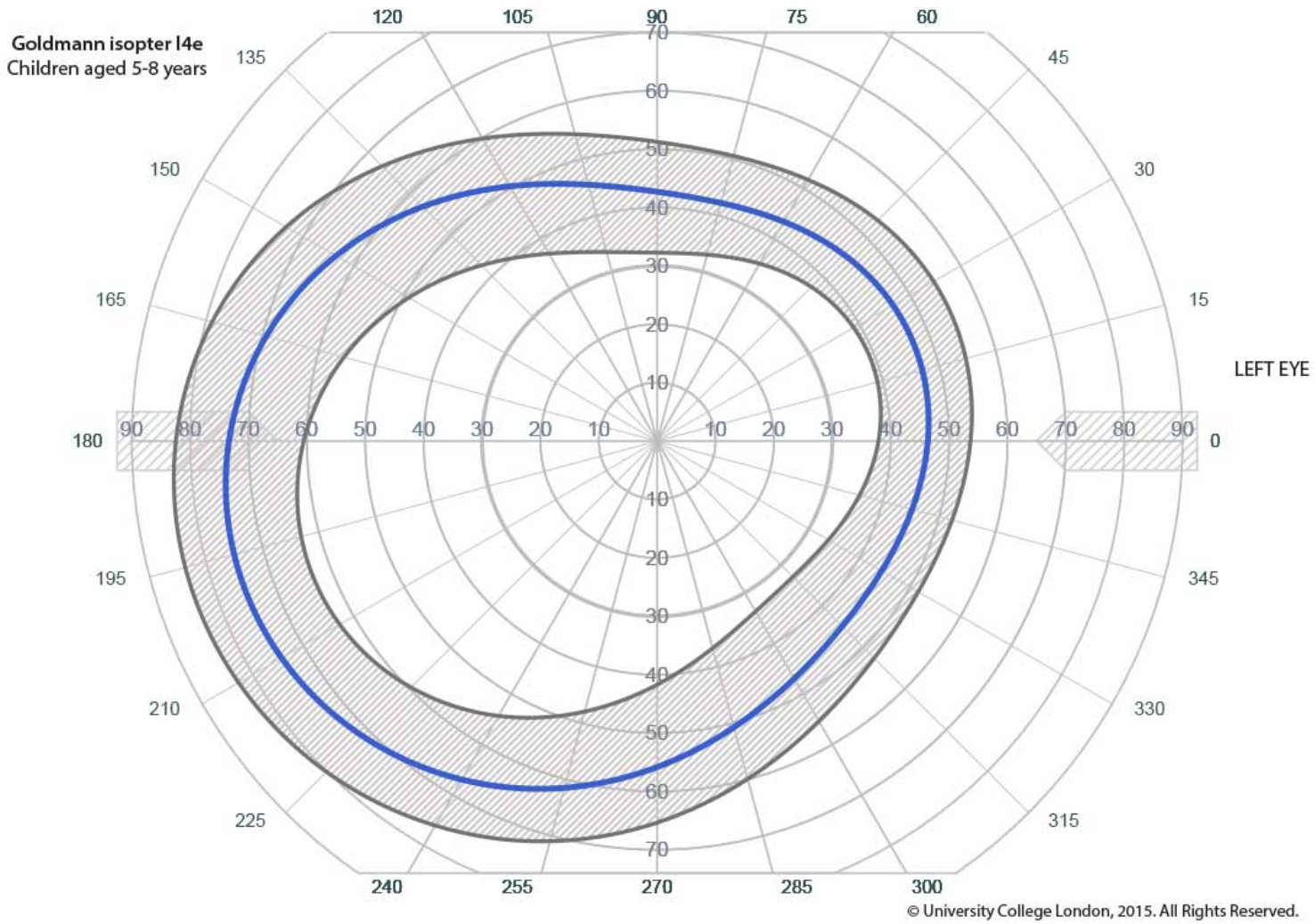

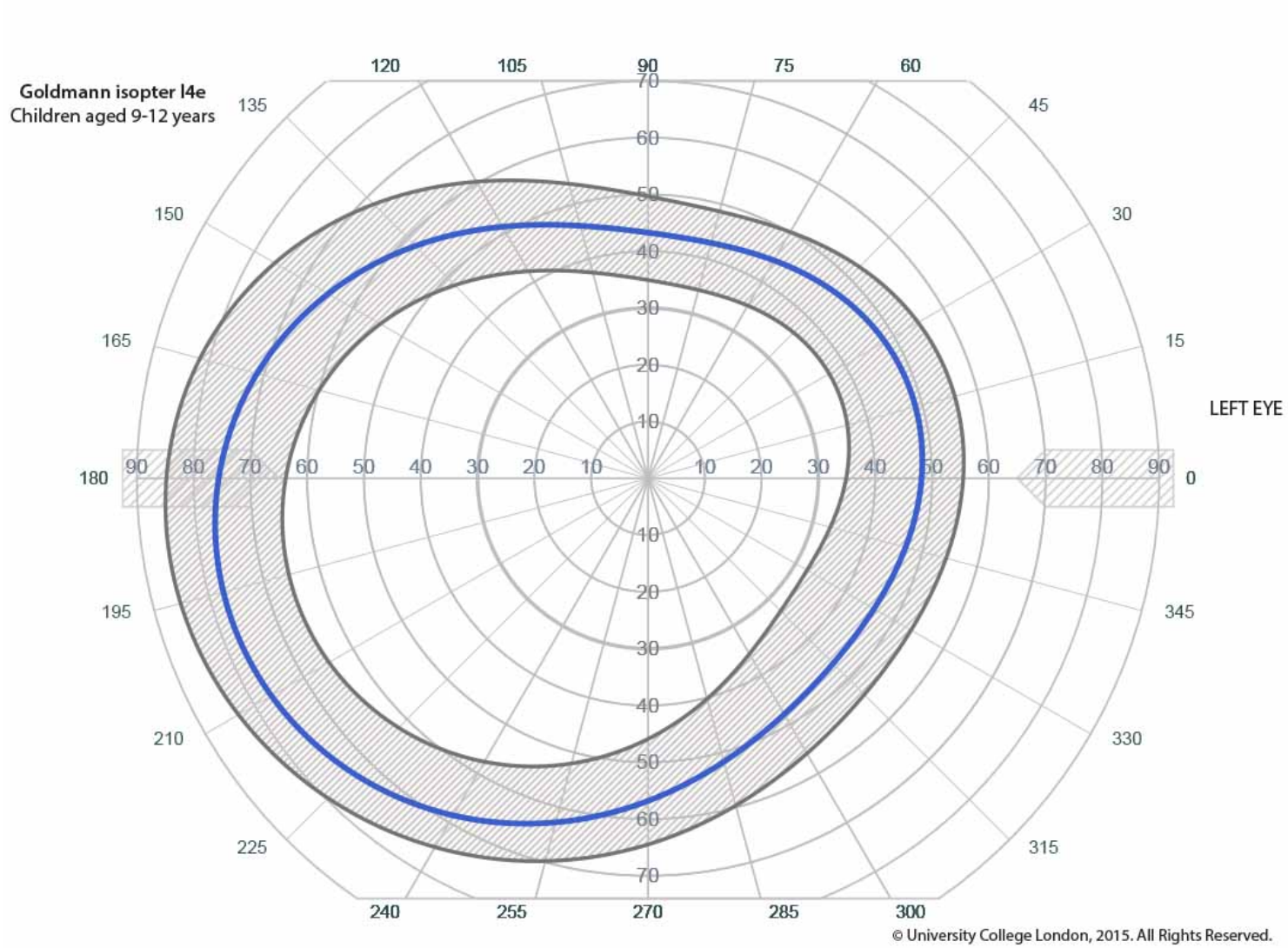
Goldmann isopter I4e
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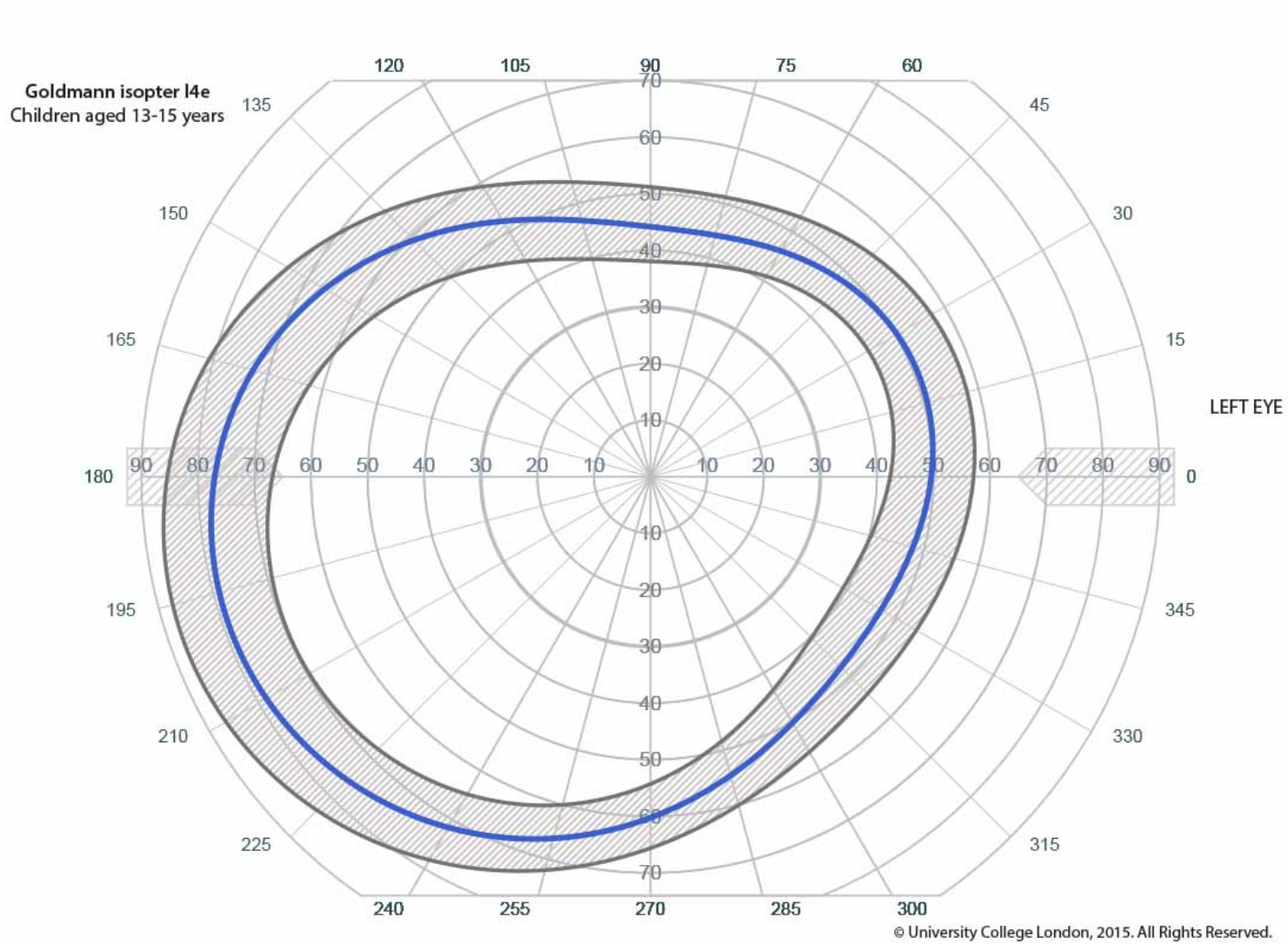

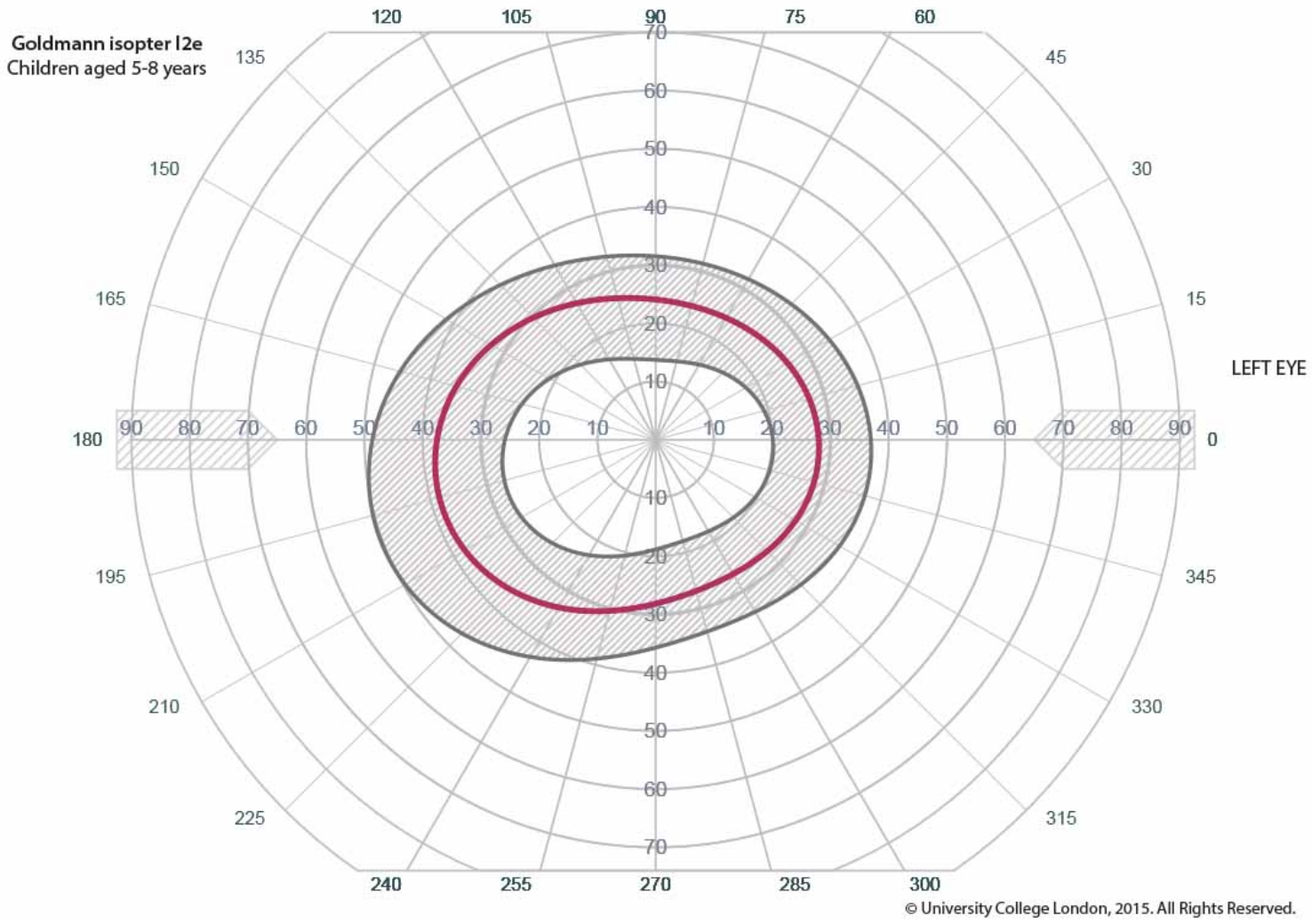
Goldmann isopter I2e
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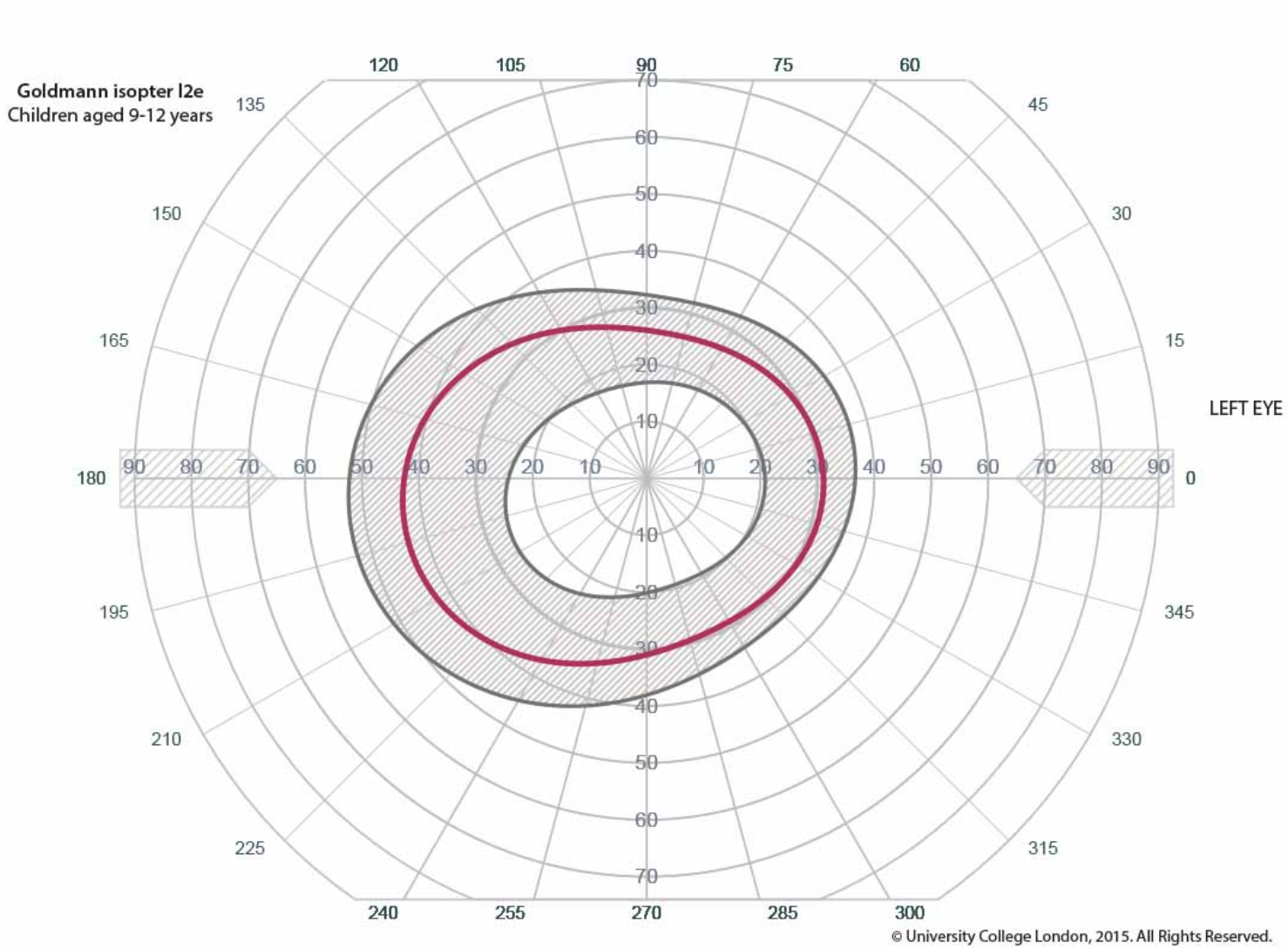
Goldmann isopter I2e
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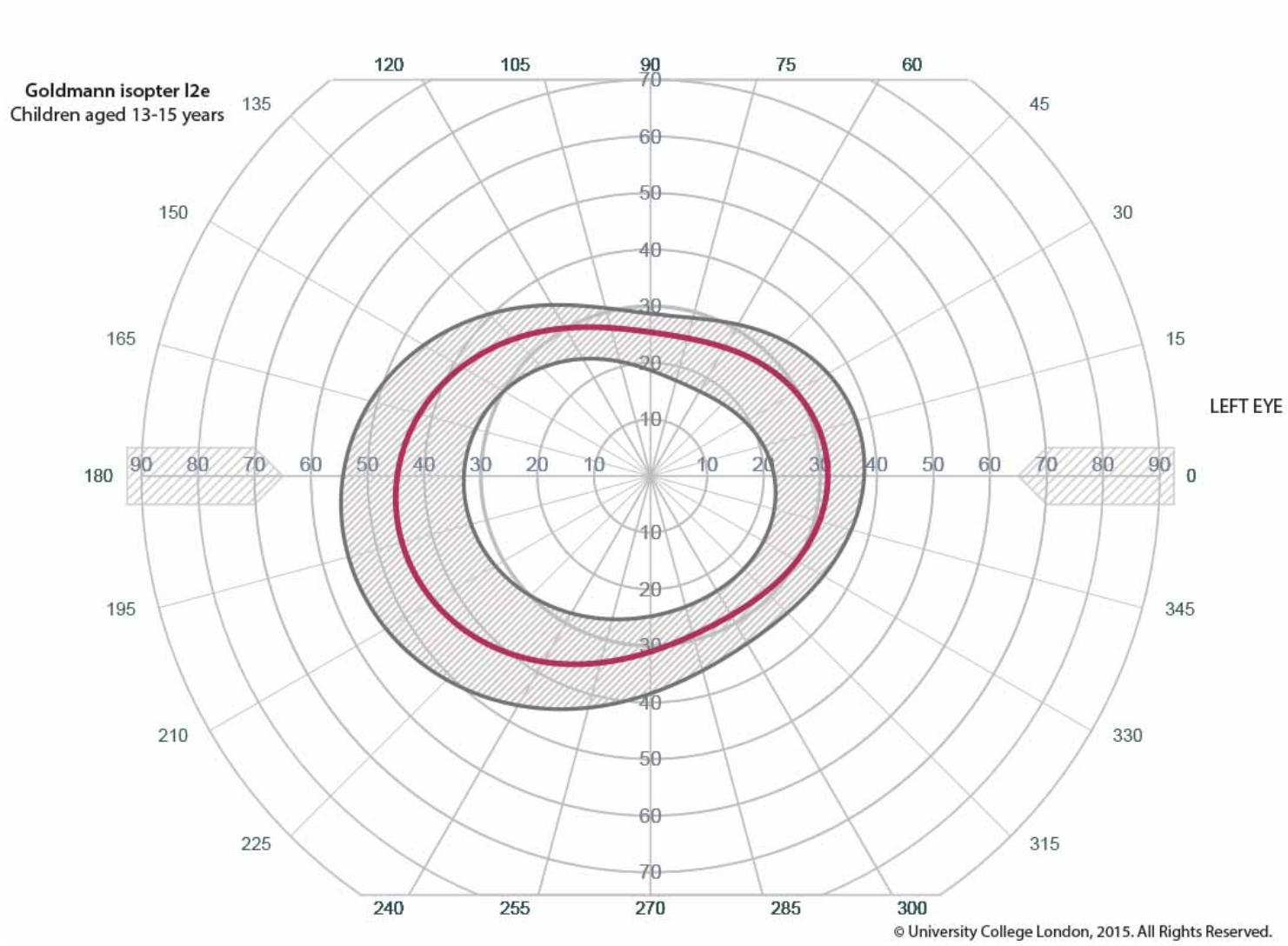
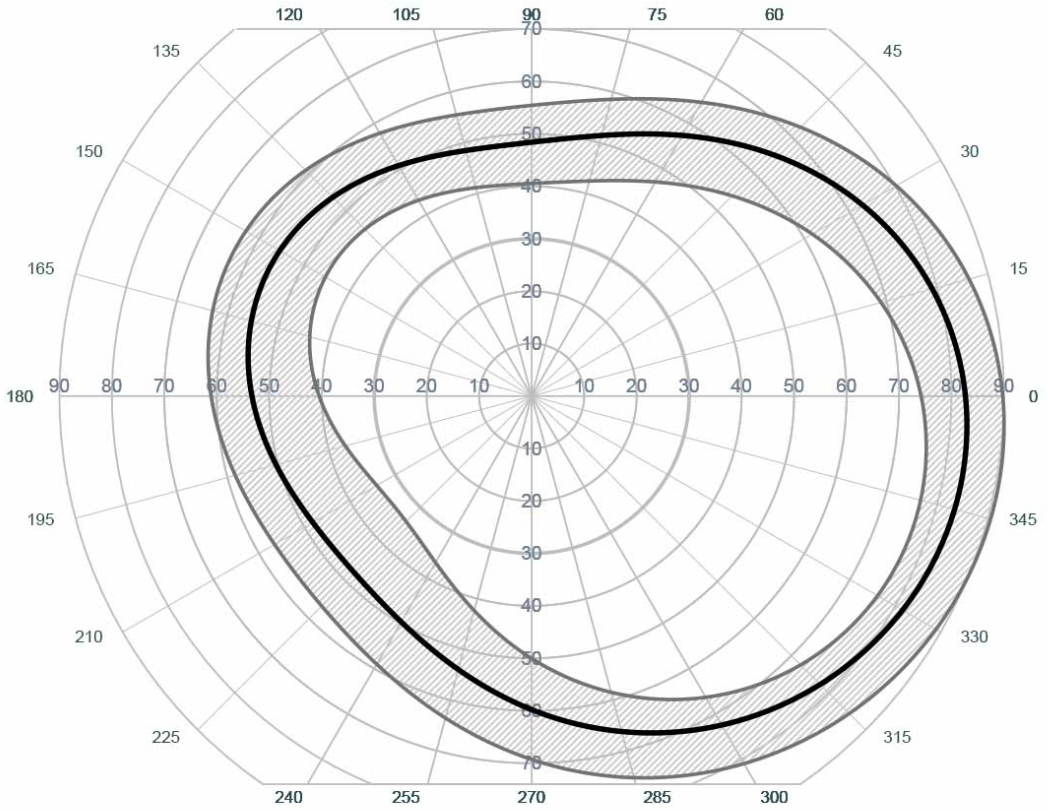


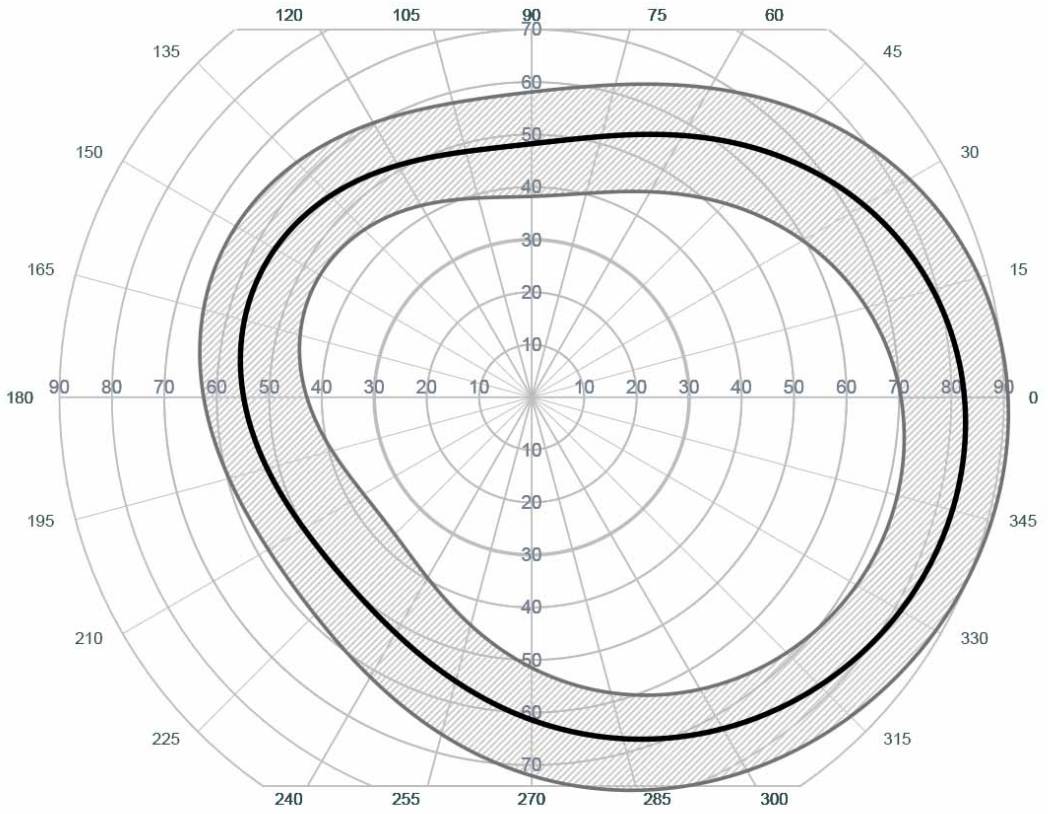
Octopus isopter III4e
Children aged 5-8 years

RIGHT EYE



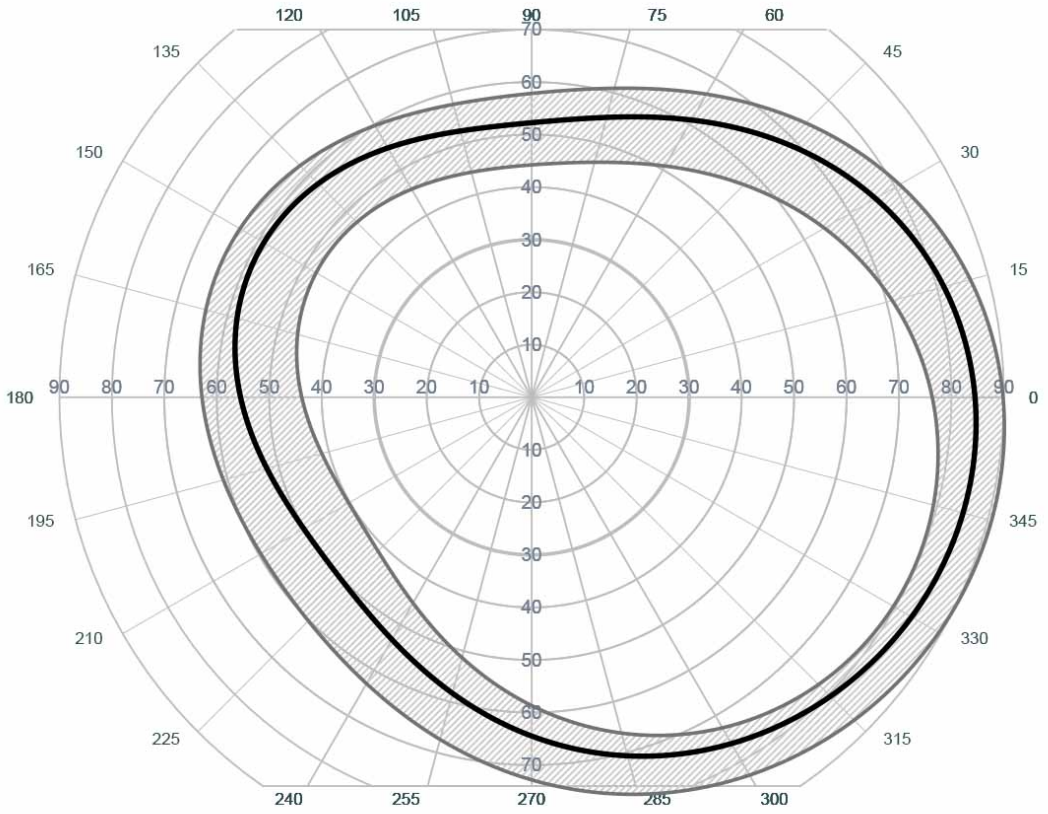
Octopus isopter III4e
Children aged 9-12 years

RIGHT EYE



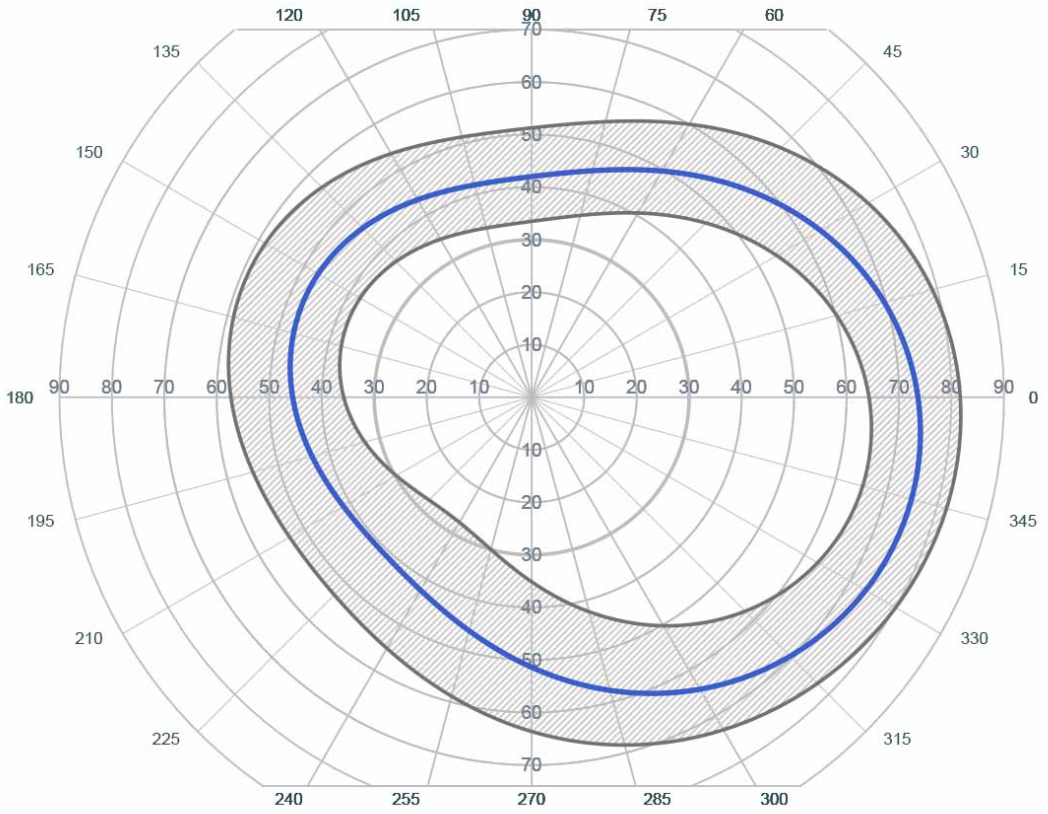
Octopus isopter III4e
Children aged 13-15 years

RIGHT EYE



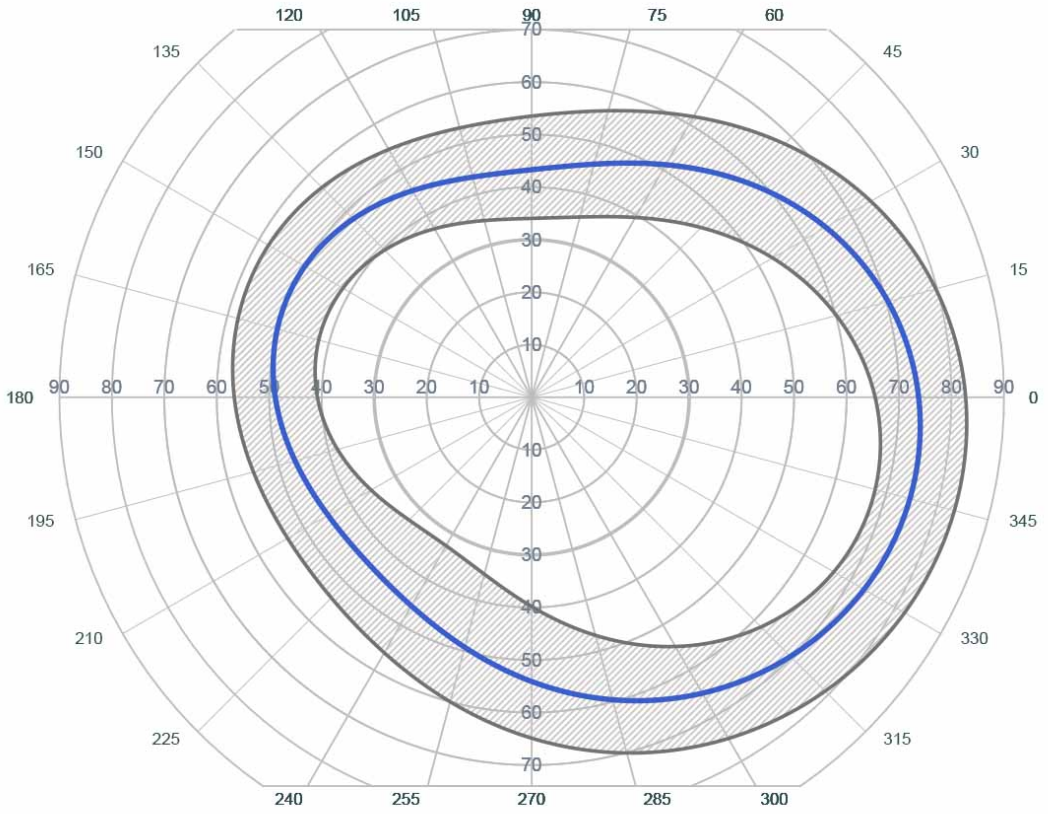
Octopus isopter I4e
Children aged 5-8 years

RIGHT EYE



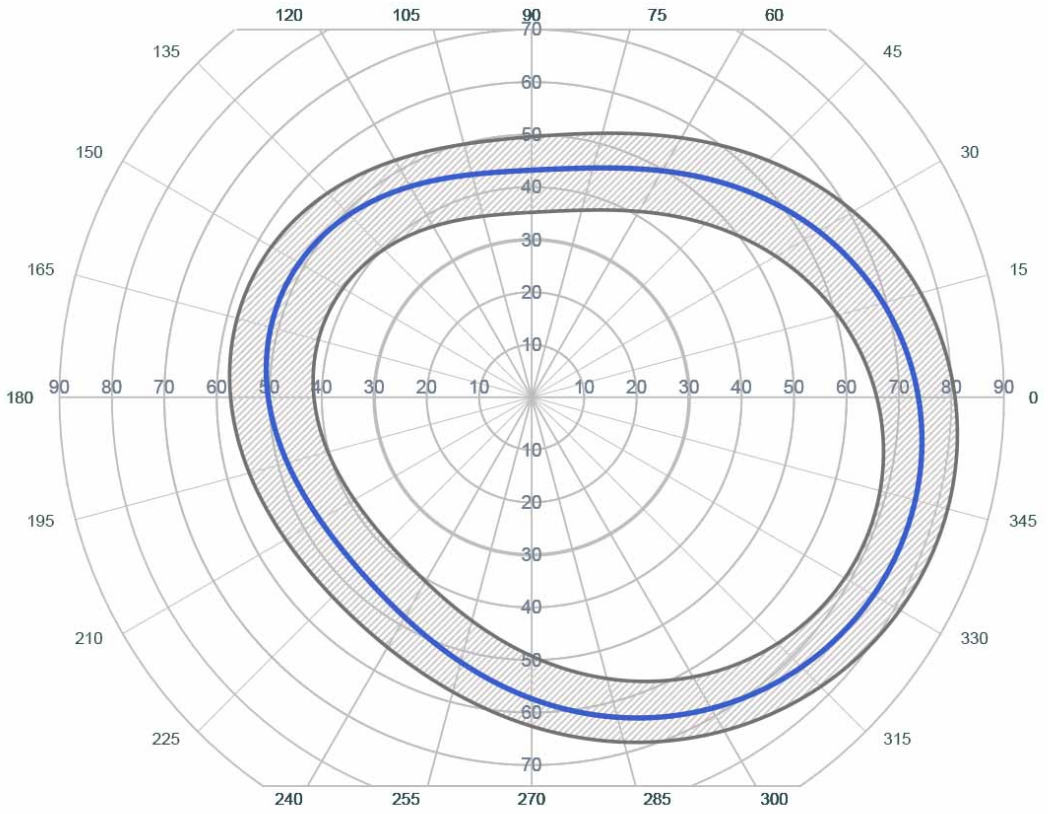
Octopus isopter I4e
Children aged 9-12 years

RIGHT EYE



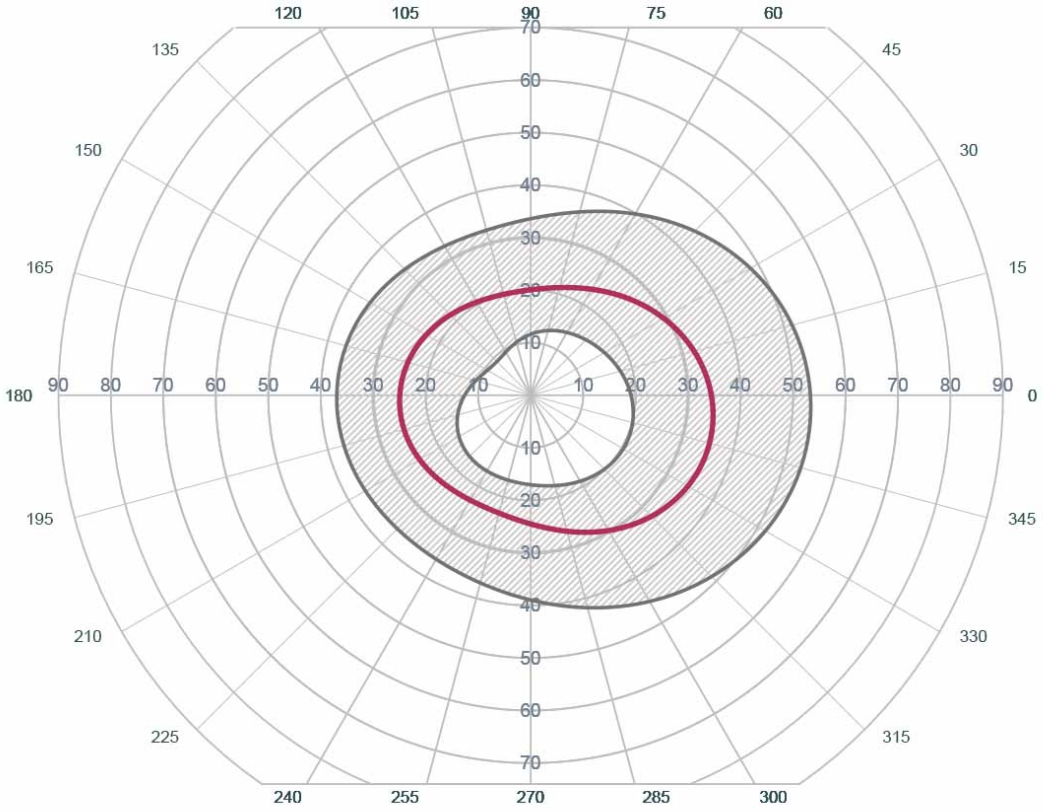
Octopus isopter I4e
Children aged 13-15 years

RIGHT EYE



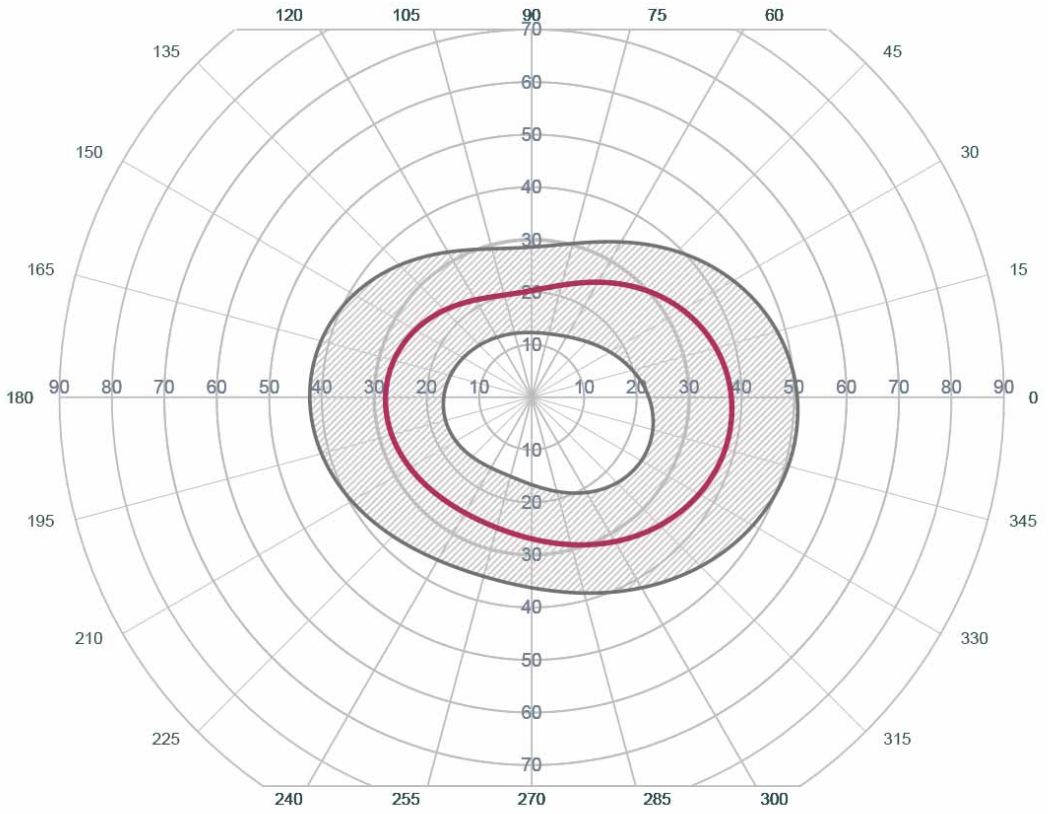
Octopus isopter I2e
Children aged 5-8 years

RIGHT EYE



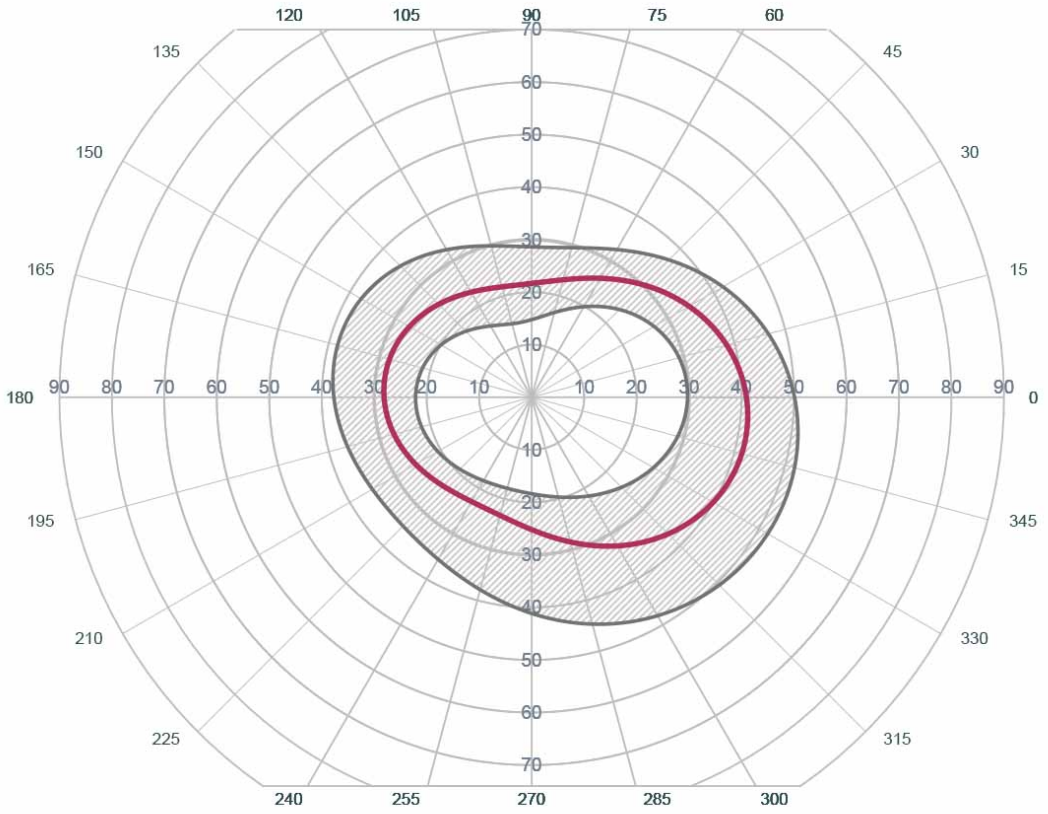
Octopus isopter I2e
Children aged 9-12 years

RIGHT EYE



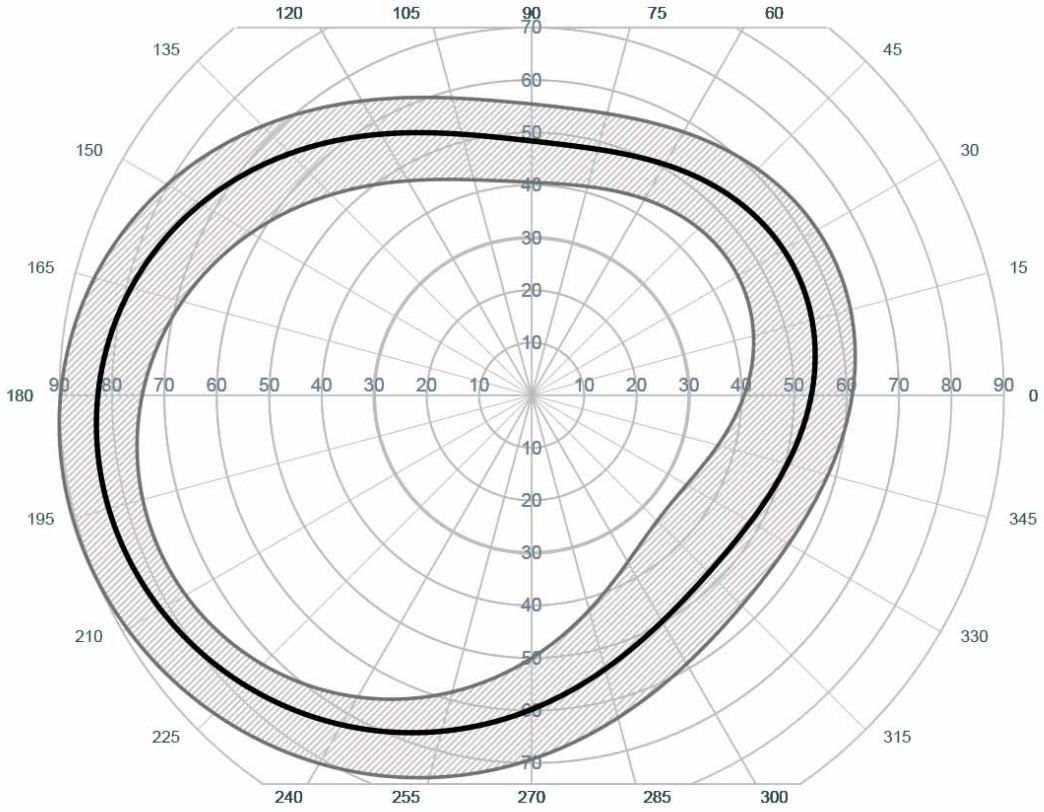
Octopus isopter I2e
Children aged 13-15 years

RIGHT EYE



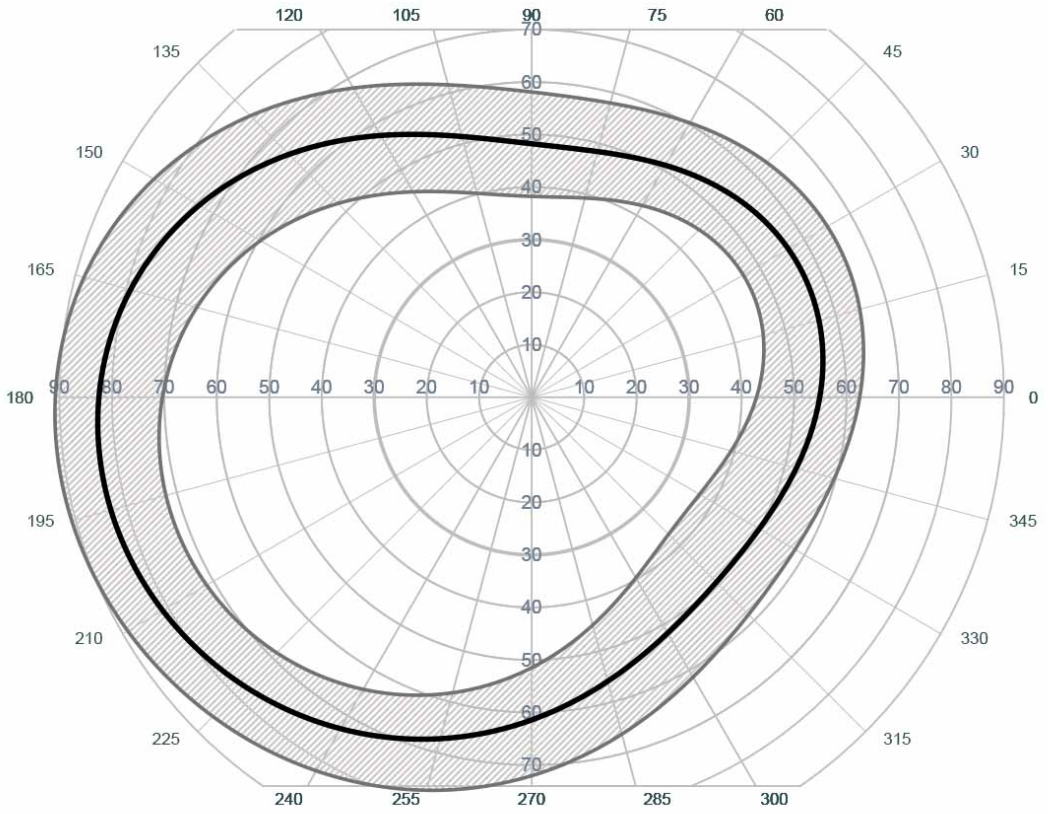
Octopus isopter III4e
Children aged 5-8 years

LEFT EYE



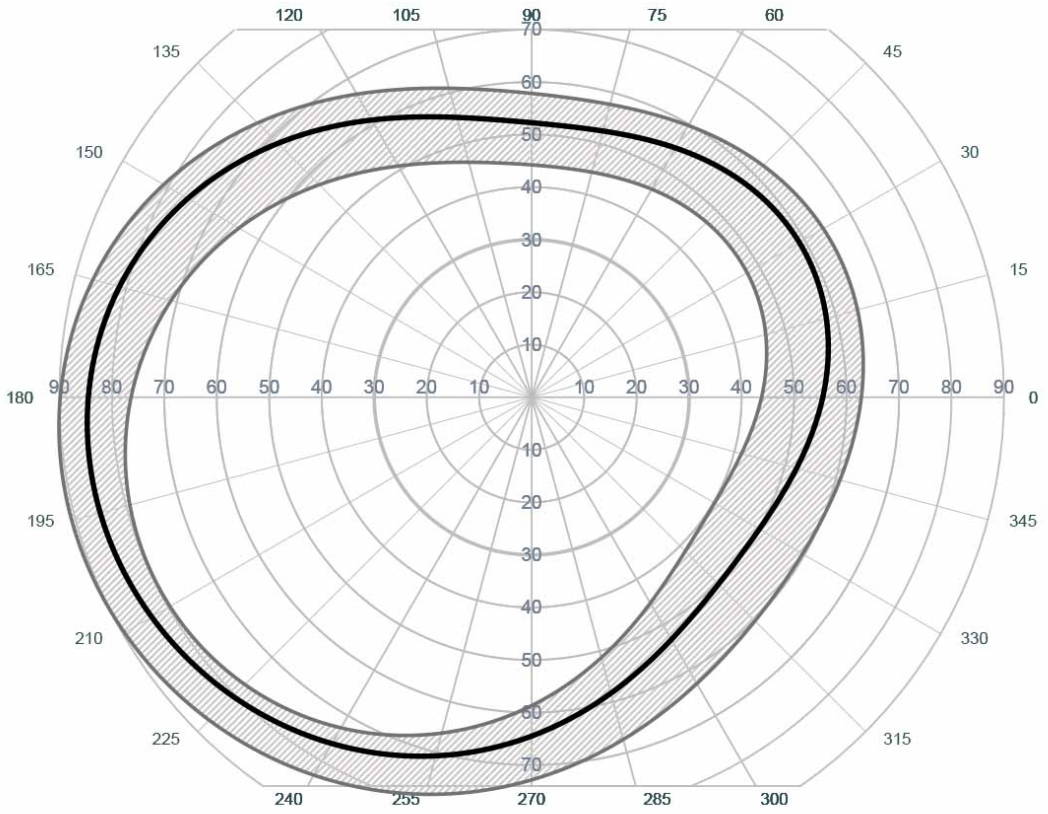
Octopus isopter III4e
Children aged 9-12 years

LEFT EYE



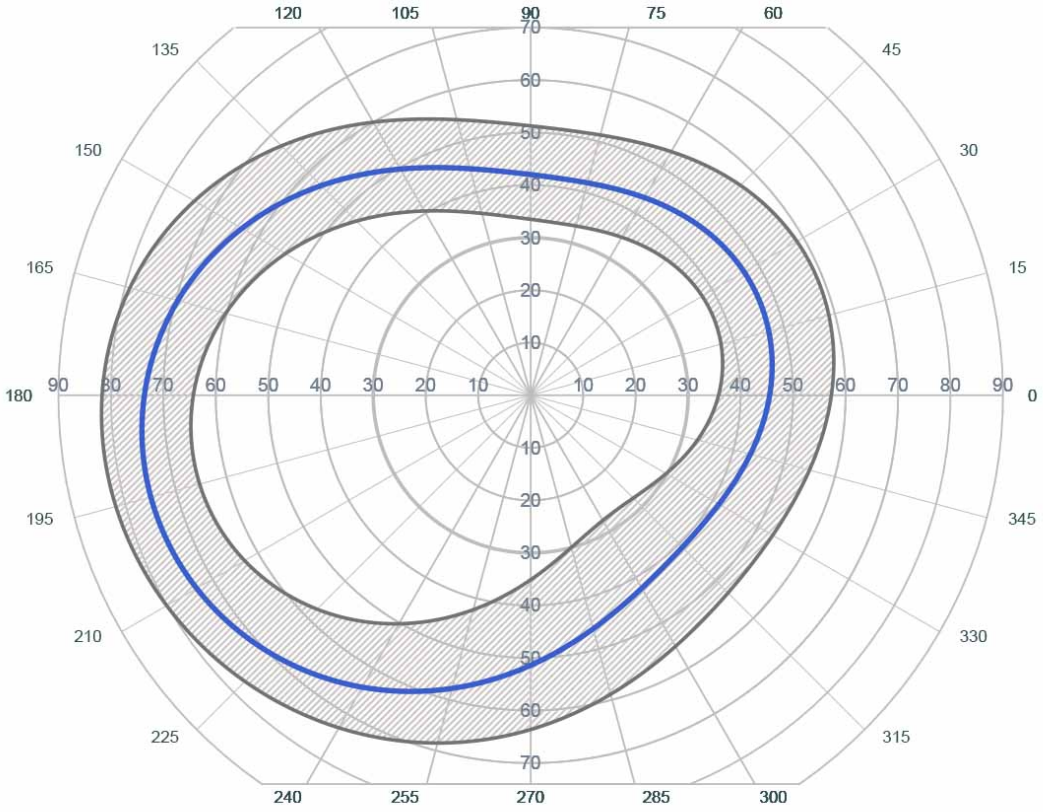
Octopus isopter III4e
Children aged 13-15 years

LEFT EYE



Octopus isopter I4e
Children aged 5-8 years

LEFT EYE



Octopus isopter I4e
Children aged 9-12 years

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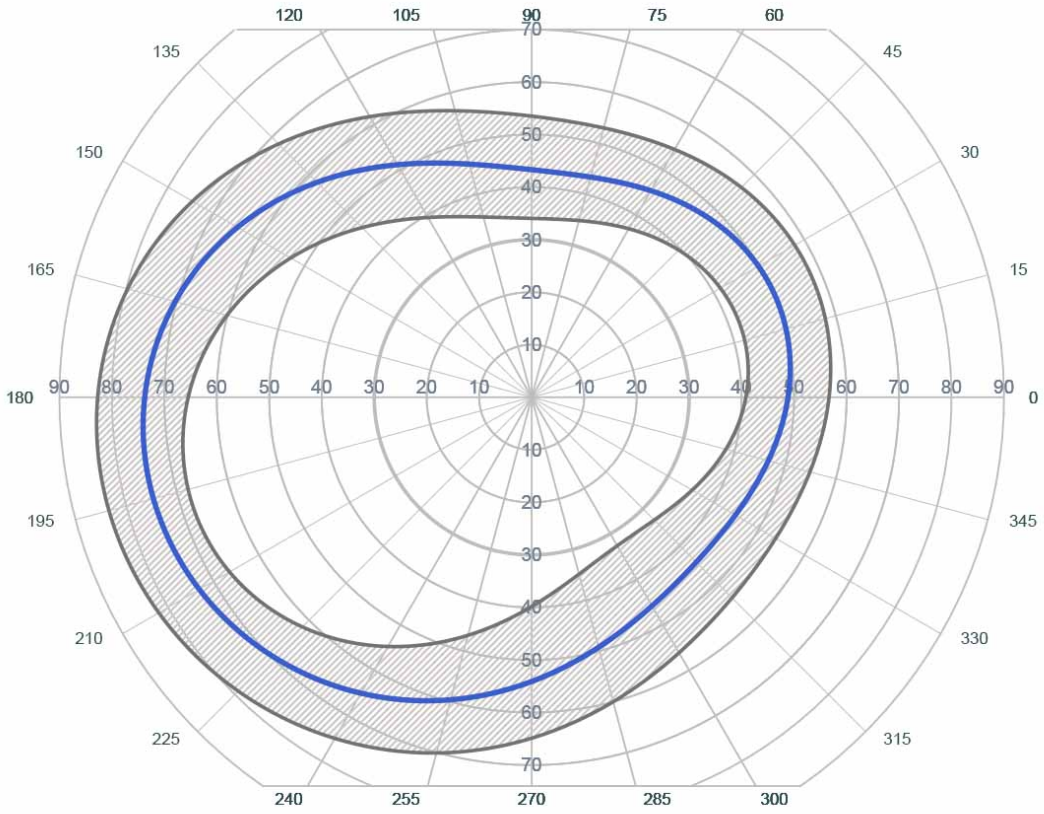
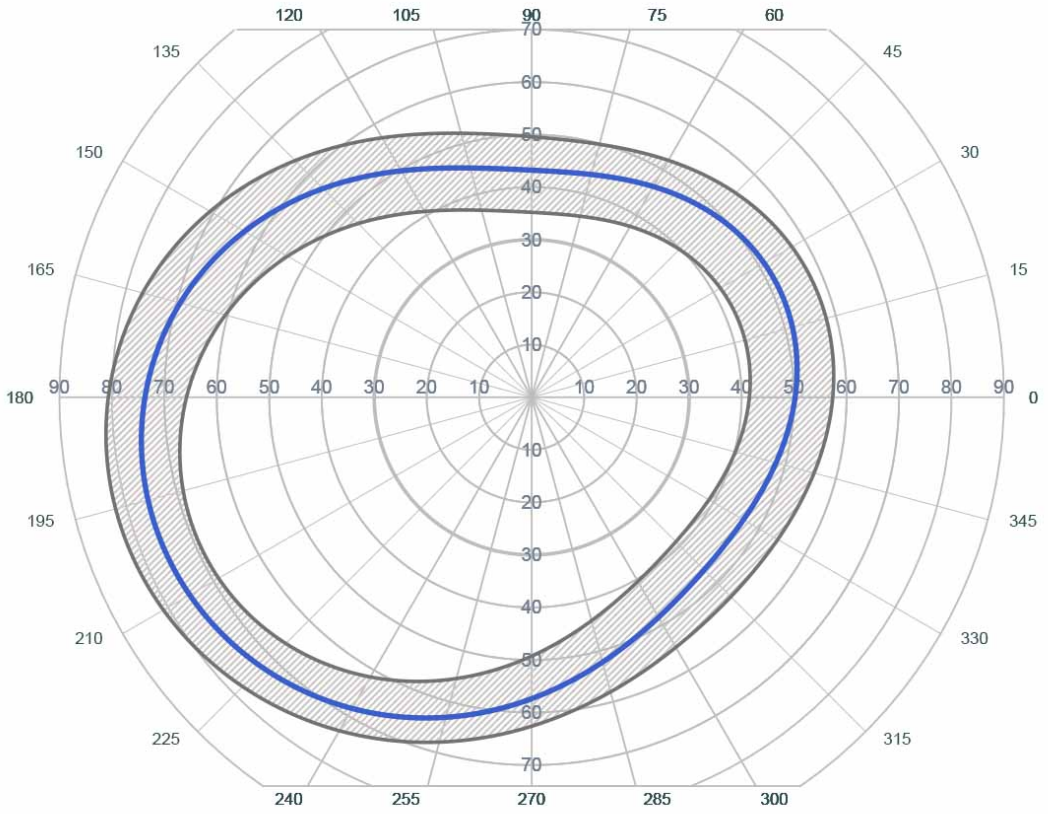


Octopus isopter I4e
Children aged 13-15 years

LEFT EYE



Octopus isopter I2e
Children aged 5-8 years

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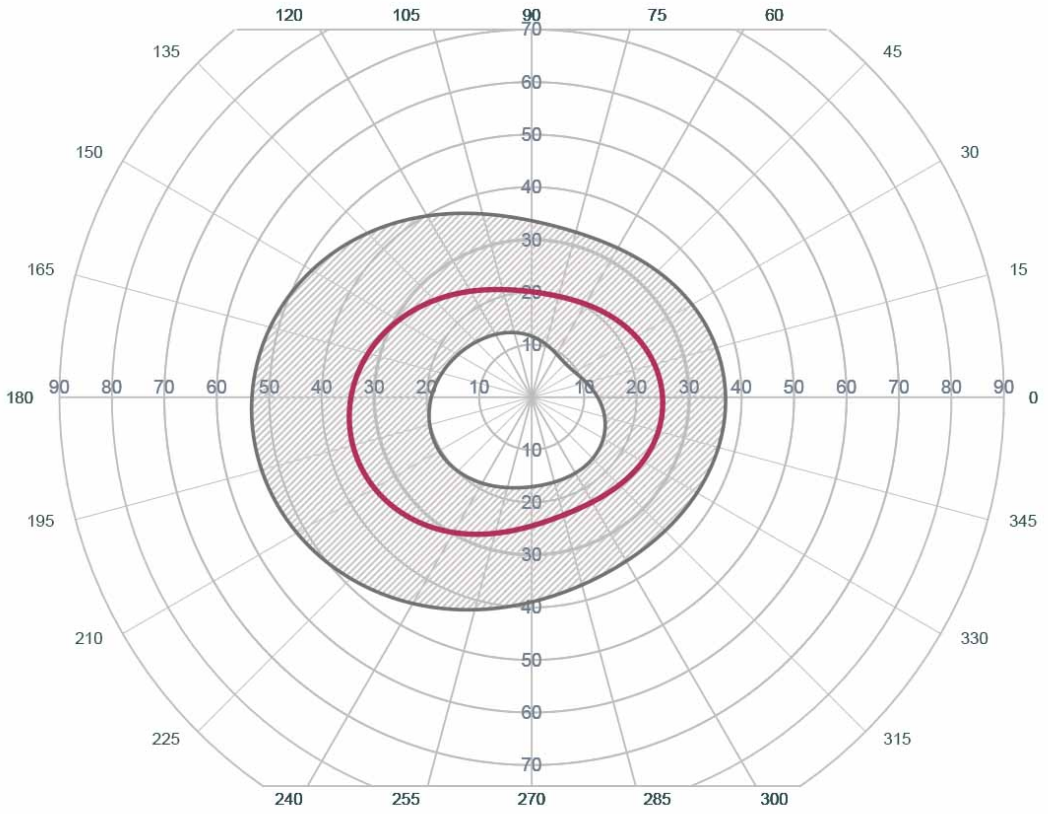

Octopus isopter I2e
Children aged 9-12 years

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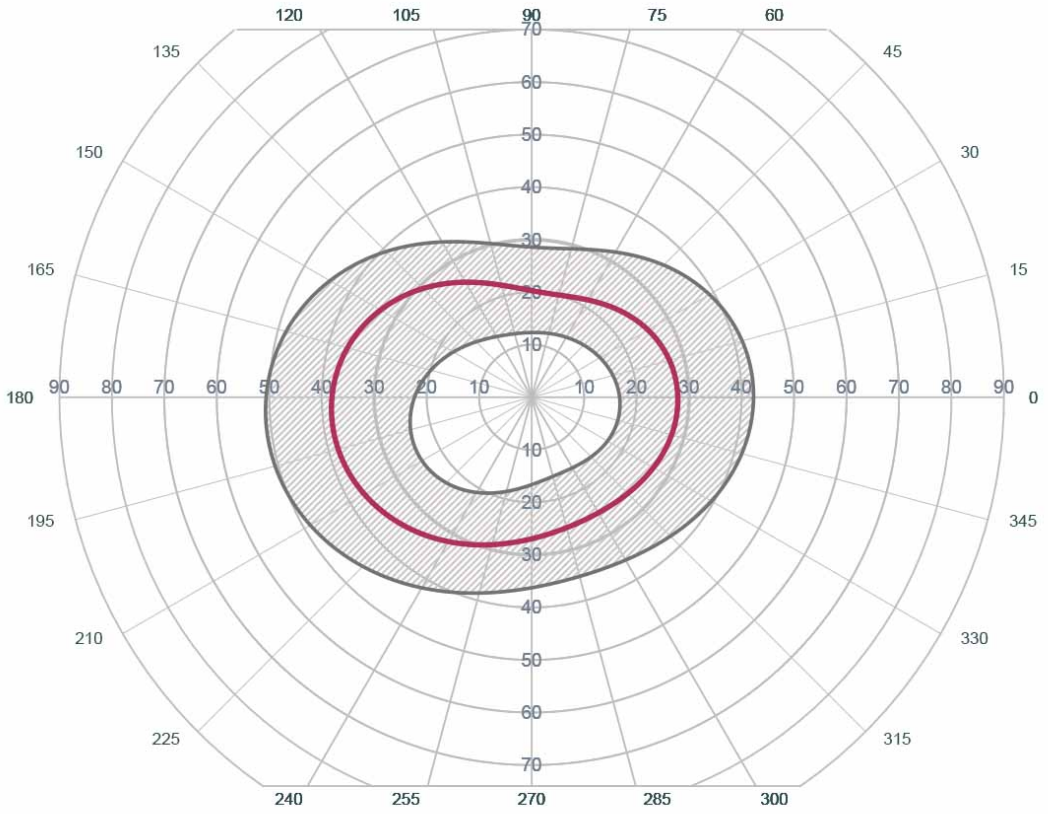

Octopus isopter I2e
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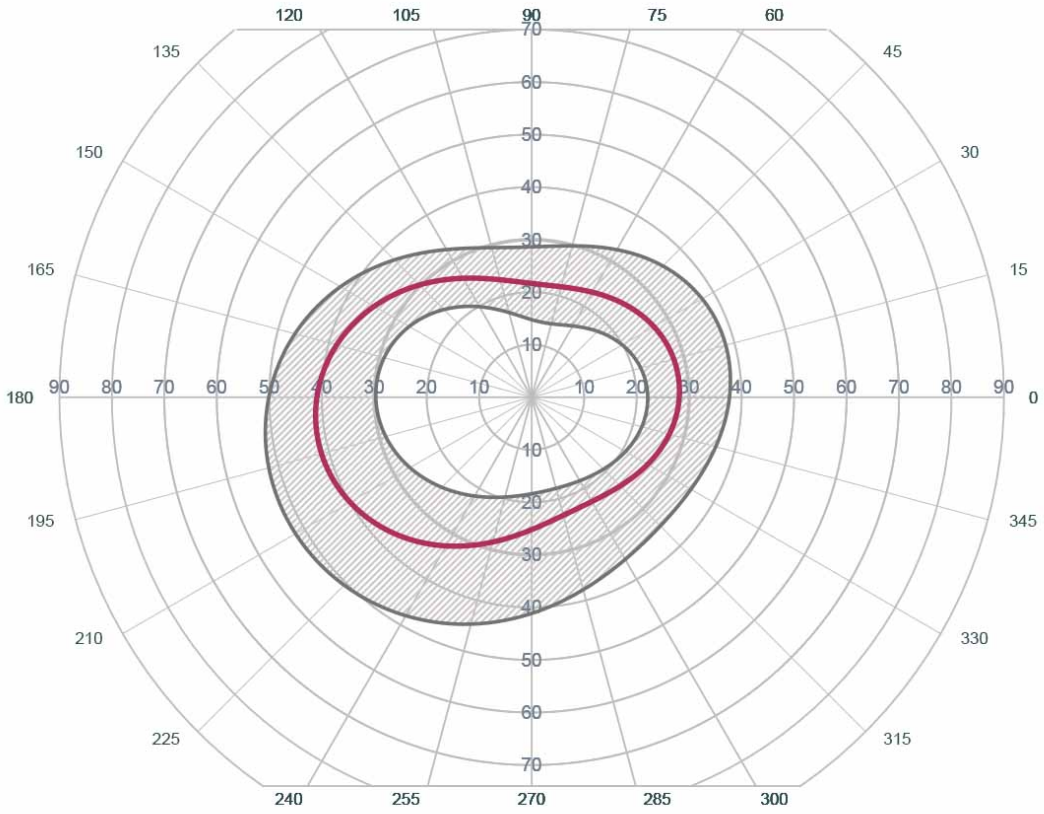

9.8.4 Perimetry in children – standard operating procedures (SOPs)

9.8.4.1 Childhood glaucoma

Visual Field Testing SOP

Childhood glaucoma

Childhood glaucoma is a relatively rare, potentially blinding eye condition characterised by elevated intraocular pressure (IOP) and optic nerve damage. Primary glaucoma is most often managed surgically, and patients undergo lifelong follow-up to monitor progress. Assessment of the visual field provides information regarding disease status, and can be useful in the monitoring of disease progression.

The assessment of visual fields in children relies on the subject understanding the task and cooperating with the test procedure. Thus, children should be comfortable, informed and engaged throughout testing.

To facilitate this, assessments should be short, allow for rest breaks, and utilise an adaptive protocol determined by the limits of an individual child's capability.

The following guidelines, based primarily on findings from the Study of Optimal Perimetric Testing In Children (OPTIC study), set out general visual field testing instructions and the *minimum* expected outcome in children, split by age group.

Overview of recommended techniques

Static perimetry
The most commonly used test in the UK is the SITA 24-2 FAST (using the Humphrey perimeter). Other techniques include the SITA standard and Octopus G-TOP – all of which can be used successfully to detect glaucomatous damage in children.

Once a test strategy is selected, it should be used for all future tests.

Combined static and kinetic perimetry
This should only be performed in children over 10 years of age. The addition of a kinetic isopter (over standard static techniques) provides information on the full visual field (see section – Choice of kinetic stimuli for guidance).

Kinetic perimetry
Solely kinetic perimetry should be reserved for cases where:

1. Co-operation is too poor to achieve a reliable result with static perimetry.
2. There is severe visual field loss and the child is unable to complete a static assessment.

Confrontational visual fields
This technique is reserved for the very few cases where co-operation with formal perimetry is extremely limited. Confrontational testing can identify gross defects – but has limited capability in detecting small changes in visual field sensitivity.

Summary
Once a test strategy is selected, it should be used for all future tests.

Rarebit techniques are not in common use, and current evidence does not recommend the use of Saccadic Vector Optokinetic Perimetry (SVOP).

Test protocol

General points

Assessments can be undertaken on the Humphrey or Octopus 900 perimeter – using a static (or combined static/kinetic test protocol (older children only).

Unless otherwise specified, right eyes are to be examined first, followed by left eyes. Children will have the non-tested eye occluded with a soft eye pad. Following this, they should be positioned at the perimeter with seat and chin rest adjustments until aligned and comfortable. Additional padding on the chinrest to reach the correct height should be given to any child requiring it.

As soon as examination of the first eye is complete, the occlusion should be removed, and the child allowed a few minutes to rest, whilst the assessment of the second eye is prepared. Rest breaks are a useful component of a visual field assessment and should be taken at any time where the examiner deems that the quality of testing is suffering due to subject fatigue.

Rating test reliability

The Examiner Based Assessment of Reliability (EBAR)[149]

Implement the Examiner Based Assessment of Reliability (EBAR) scoring system (described below, from Patel et al, 2015) and record the result on the visual field printout.

The EBAR score is a qualitative, categorical system with outcomes of 'good', 'fair' or 'poor' quality of perimetric test. It is independent of visual field outcome. The EBAR rating has been designed and implemented to guide the evaluation of reliability in paediatric perimetry. Subjects should be assigned a score using the criteria in Box 1.

'Good' rating: Compliance with testing is good. The subject is able to maintain good central fixation and respond promptly. They may have some fixation losses at times, but are able to understand and comply well with test instructions. General behaviour allows a comprehensive assessment and overall, visual field outcome is expected to represent true visual field size/sensitivity.
'Fair' rating: Compliance with testing is mostly good. The subject may have moderate fixation losses with some variability in responses. They are able to understand test instructions and their general behaviour allows for moderate co-operation. They may show evidence of fatigue that affects performance and respond to the noise of stimulus presentation at times. Overall, visual field outcome is expected to be able to detect gross defects, but may over/under-estimate true visual field size/sensitivity.
'Poor' rating: Compliance with testing is poor. The subject demonstrates very high fixation losses or searching for stimuli. They may be unable to ignore the sound of stimulus presentation and therefore produce high false positive responses. They may also demonstrate highly variable responses, with a possible lack of understanding of test instructions. Overall, test performance is not expected to represent true visual field size/sensitivity and results will be unable to rule-in or rule-out visual field defects.

Box 1. Examiner Based Assessment of Reliability (EBAR) scoring system

The Kinetic Perimetry Reliability Measure (KPRM)

NOTE: This is only used for kinetic perimetry.

KPRM is based on plotting four final points at the very end of a kinetic assessment using the outer-most isopter stimulus already used in the test. One point is plotted in each quadrant along a randomly selected meridian (that has already been used for plotting that original isopter). KPRM points are not repeated if the subject loses concentration during this phase of the test. Taking a median value of the distance (in degrees) between these four KPRM points and the points previously plotted on the outer isopter line gives a KPRM score and this score is used as a proxy to quantify reliability (Figure 2).

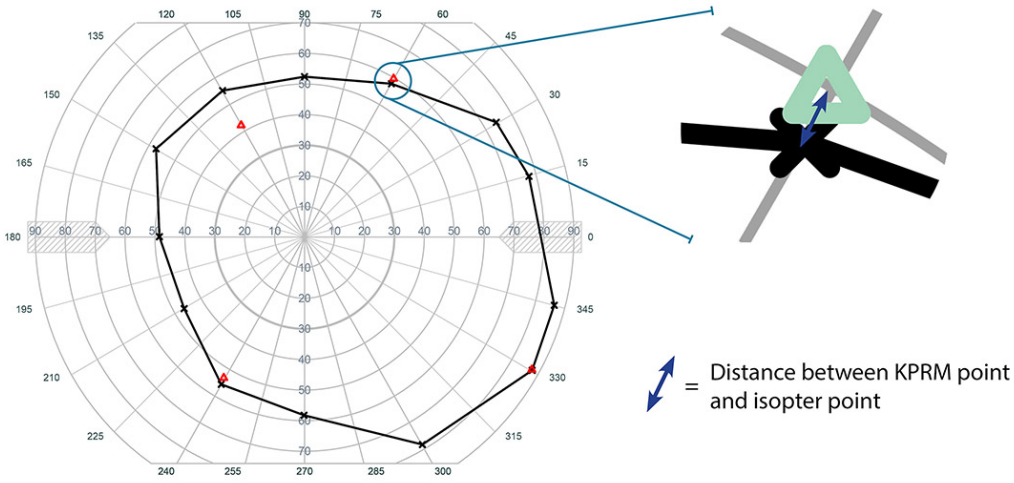

Figure 2. KPRM points (triangles) and distance between corresponding points (arrow)

KPRM points should be marked on the visual field printout using a coloured pen.

Static perimetry

If using the Humphrey perimeter, use gaze-tracking and blind spot monitoring using the Heijl-Krakau method. For Octopus perimetry, turn off the automated realignment system.

Correction of refractive errors
Errors of ≥ +3.00 dioptre spheres (DS), ≥ -1.00DS, and > ±1.00 dioptre cylinders (DC) should be fully corrected using large aperture lenses.[15]

Clear instructions
Instructions to patients have a significant effect on reliability and repeatability. This can be minimised by clear instructions to the patients by the perimetrist as to what is to be done and how they should respond. These should be given before each test.

> "We're going to look at the green [or white] light in the middle of the bowl. For the test, you need to watch the green [or white] light all the time and try not to look anywhere else. There will be a little white light that flashes somewhere in the bowl [point to peripheral areas within the bowl], and you just need to press your buzzer as soon as you see the light. The light can be really bright, or quite hard to see."

[Confirm instructions have been understood]

> "Can you test the buzzer for me now?"

[Subject presses buzzer]

Set the child in the correct position, and begin the assessment.

Kinetic perimetry

Choice of kinetic stimuli

A choice of stimuli from isopters V4e, III4e, or I4e can be used. Table 1 gives an illustration of potential isopter choice.

Table 1. Choice of isopter stimulus dependent on central visual acuity

Central visual acuity (LogMAR)	Test isopters
>1.3 (3/60 Snellen equivalent)	V4e
0.8 to 1.2	III4e
0.3 to 0.7	I4e (III4e if I4e not seen)
<0.2 (6/9.5 Snellen equivalent)	I4e

Correction of refractive error

No correction should be applied.[70]

Test protocol

Prior to testing, the child will undergo three practice presentations using the test stimulus. Practice points will not be used to form the test isopter.

For the test, targets are to be presented in a random order along 12 cardinal meridians (every 30°, Figure 1), centripetally (peripheral location to central) from a **non-seeing** area using the testing protocol adapted from Werner.[14] Test points should be started at manually plotted locations, with an automated speed of 5°/sec.[35]

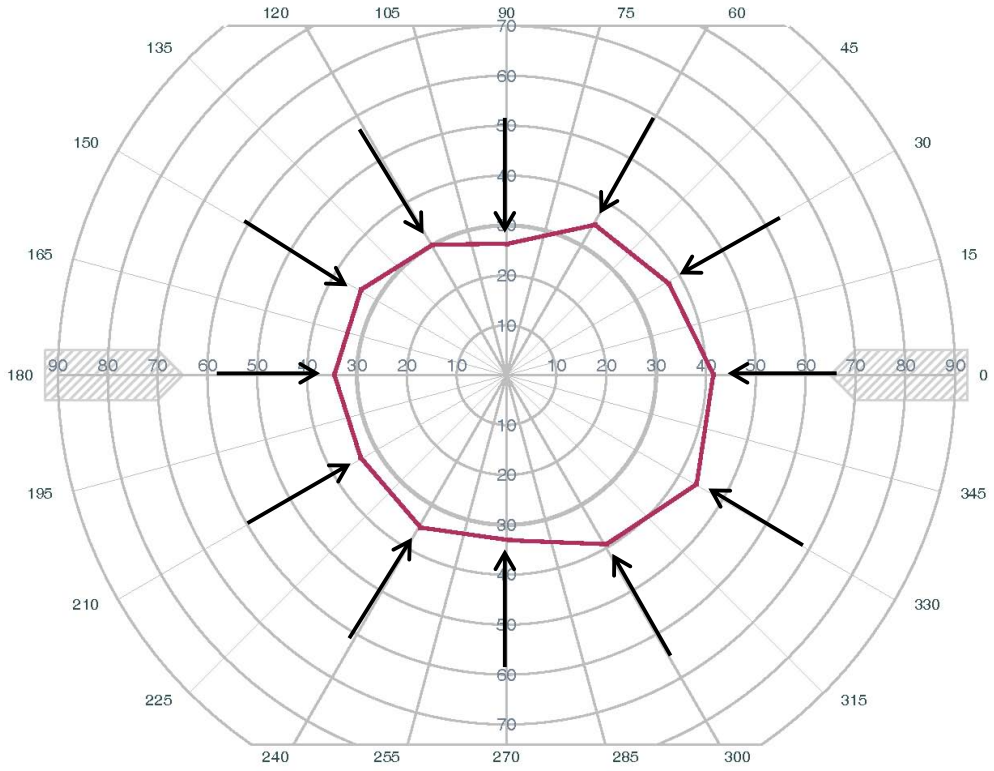

Figure 1. Presentation of stimuli every 30°

For those children who can tolerate further testing, additional points can be tested, in a non-randomised order along meridians 15° adjacent to the cardinal points starting with nasal field locations. This 'filling in' between test points allows for more accurate plotting of visual field shape, up to a maximum of 24 points per isopter.

Test points can be re-plotted if the examiner feels the initial response is unreliable i.e. the child loses fixation during the stimulus presentation, searches for stimuli, fails to respond or presses for the noise of stimulus presentation. This accommodates temporary lapses in co-operation, but repeat testing should not be undertaken in those with persistently poor co-operation.

Clear instructions

Instructions to patients have a significant effect on reliability and repeatability. This can be minimised by clear instructions to the patients by the perimetrist as to what is to be done and how they should respond. These should be given before each test.

> "We're going to look at the green [or white] light in the middle of the bowl. For the test, you need to watch the green [or white] light all the time and try not to look anywhere else. There will be a little white light that looks like this (demonstrate stimulus), that moves in from the side, and you just need to press your buzzer as soon as you see the light."

[Confirm instructions have been understood]

> "Can you test the buzzer for me now?"

[Subject presses buzzer]

Set child in the correct position, and begin familiarisation task.

> "We're going to start with a quick practice, so you know what to look for."

[Inform child when test begins]

Allow the child to "sit back and relax" between assessments.

The following sections highlight potential changes in test procedure for children of different ages.

Children aged 5-7 years

In this age group, you should expect to plot 12-15 points per isopter.

Approximately 40% of children will be able to achieve a 'good quality' EBAR test rating.

Children aged 8-12 years

In this age group, you should expect to 18-24 points per isopter.

Approximately 75-80% of children will be able to achieve a 'good quality' EBAR test rating.

Children aged 13+ years

In this age group, you should expect to 18-24 points per isopter and subjects will demonstrate adult-like responses. Isopter choice should allow for maximum coverage of the visual field.

Almost every child should be able to achieve a 'good quality' EBAR test rating.

Interpretation of findings

Classification of field defects can aid monitoring of conditions – for both communicating with patients/families and monitoring change with time (see Table 2, below).

Table 2. Classification of glaucomatous visual field defects[134]

Stage I	Only relative defects.
Stage II	Spot-like, stroke-like, or arcuate absolute defects, having no connection to the blind spot.
Stage III	Arcuate absolute defects already connected to the blind spot, with or without a nasal break-through into the periphery.
Stage IV	Extensive ring-shaped or half ring-shaped defects, with a central island of sensitivity maintained.
Stage V	Central island collapse, with only the temporal visual field area remaining.

Childhood glaucomas have been noted to share similar patterns of visual field damage to adult open-angle glaucoma, and thus adult classification systems can be similarly used in children. However, when interpreting fields, it is vital to recognise the role of test reliable and weight the perimetric findings accordingly. Those tests rated as 'poor' quality should not be used to inform clinical management. Tests rated as 'fair' quality can give an indication of the presence of visual field loss, but may cause 'noise' when attempting to monitor progressive loss, thus it is recommended that only 'good' quality tests are used for monitoring progression.

9.8.4.2 Neuro-ophthalmic disease

Visual Field Testing SOP

Children with neuro-ophthalmic disease

Neuro-ophthalmic diseases in children comprise a group of conditions which, by definition, compromise the optic nerve along the course of the visual pathway. Assessment of the visual field allows for detection of nerve damage and identifies characteristic changes in visual field shape to localise defects within the brain.

The assessment of visual fields in children relies on the subject understanding the task and cooperating with the test procedure. Thus, children should be comfortable, informed and engaged throughout testing.

To facilitate this, assessments should be short, allow for rest breaks, and utilise an adaptive protocol determined by the limits of an individual child's capability.

The following protocol sets out general visual field testing instructions and the expected outcome in children, split by age group.

Overview of recommended techniques

Assessments can be undertaken on a Goldmann or Octopus 900 perimeter – using a kinetic test protocol. These children may be undergoing active treatment for their underlying neurological condition, in which case they will be acutely unwell, and testing will be difficult. Rest breaks are a useful component of a visual field assessment and should be taken at any time where the examiner deems that the quality of testing is suffering due to subject fatigue.

Test Protocol

Choice of stimuli

A choice of stimuli from isopters V4e, III4e, I4e and I2e can be used. Table 1 gives an illustration of potential isopter choice.

Central visual acuity (LogMAR)	Test isopters
>1.3 (3/60 Snellen equivalent)	V4e and III4e
0.8 to 1.2	III4e and I4e
0.3 to 0.7	III4e and I2e (I3e if I2e not seen)
<0.2 (6/9.5 Snellen equivalent)	I4e and I2e

Table 1. Choice of isopter stimulus dependent on central visual acuity

Correction of refractive error

No correction should be applied for isopters V4e, III4e, or I4e.[70] For isopter I2e, errors of ≥ +3.00 dioptre spheres (DS), ≥ -1.00DS, and > ±1.00 dioptre cylinders (DC) should be fully corrected using large aperture lenses.[15]

Rating test reliability

The Examiner Based Assessment of Reliability (EBAR)[149]

Implement the Examiner Based Assessment of Reliability (EBAR) scoring system (described below, from Patel et al, 2015) and record the result on the visual field printout.

The EBAR score is a qualitative, categorical system with outcomes of 'good', 'fair' or 'poor' quality of perimetric test. It is independent of visual field outcome. The EBAR rating has been designed and implemented to guide the evaluation of reliability in paediatric perimetry. Subjects should be assigned a score using the criteria in Box 1.

'Good' rating: Compliance with testing is good. The subject is able to maintain good central fixation and respond promptly. They may have some fixation losses at times, but are able to understand and comply well with test instructions. General behaviour allows a comprehensive assessment and overall, visual field outcome is expected to represent true visual field size/sensitivity.
'Fair' rating: Compliance with testing is mostly good. The subject may have moderate fixation losses with some variability in responses. They are able to understand test instructions and their general behaviour allows for moderate co-operation. They may show evidence of fatigue that affects performance and respond to the noise of stimulus presentation at times. Overall, visual field outcome is expected to be able to detect gross defects, but may over/under-estimate true visual field size/sensitivity.
'Poor' rating: Compliance with testing is poor. The subject demonstrates very high fixation losses or searching for stimuli. They may be unable to ignore the sound of stimulus presentation and therefore produce high false positive responses. They may also demonstrate highly variable responses, with a possible lack of understanding of test instructions. Overall, test performance is not expected to represent true visual field size/sensitivity and results will be unable to rule-in or rule-out visual field defects.

Box 1. Examiner Based Assessment of Reliability (EBAR) scoring system

The Kinetic Perimetry Reliability Measure (KPRM)

KPRM is based on plotting four final points at the very end of a kinetic assessment using the outer-most isopter stimulus already used in the test. One point is plotted in each quadrant along a randomly selected meridian (that has already been used for plotting that original isopter). KPRM points are not repeated if the subject loses concentration during this phase of the test. Taking a median value of the distance (in degrees) between these four KPRM points and the points previously plotted on the outer isopter line gives a KPRM score and this score is used as a proxy to quantify reliability (Figure 2).

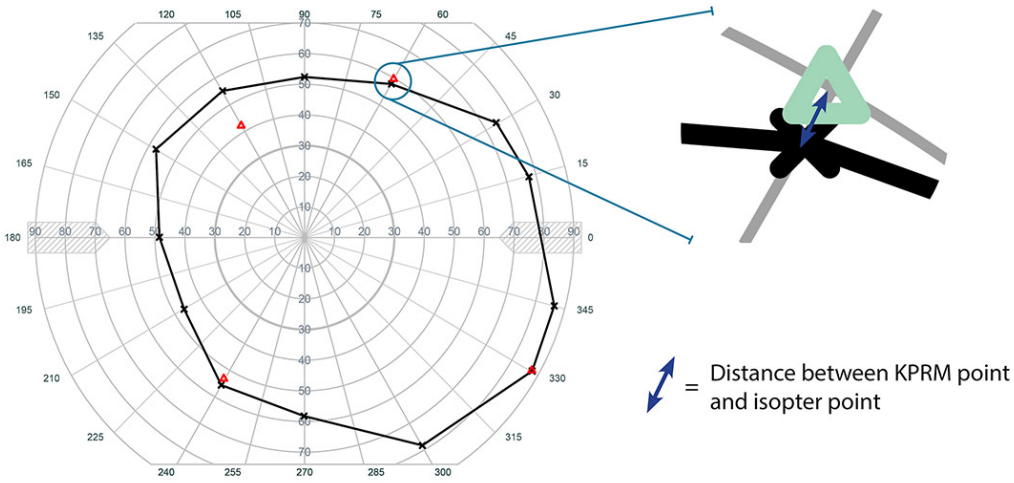

Figure 2. KPRM points (triangles) and distance between corresponding points (arrow)

KPRM points should be marked on the visual field printout using a coloured pen.

Test protocol

Unless otherwise specified, right eyes are to be examined first, followed by left eyes. Children will have the non-tested eye occluded with a soft eye pad. Following this, they should be positioned at the perimeter with seat and chin rest

adjustments until aligned and comfortable. Additional padding on the chinrest to reach the correct height should be given to any child requiring it.

Prior to testing, the child will undergo three practice presentations using the first (largest/brightest) test stimulus. Practice points will not be used to form the test isopter.

For the test, targets are to be presented in a random order along 12 cardinal meridians (every 30°, Figure 1), centripetally (peripheral location to central) from a **non-seeing** area using the testing protocol adapted from Werner.[14] Test points should be started at manually plotted locations, with an automated speed of 5°/sec.[35]

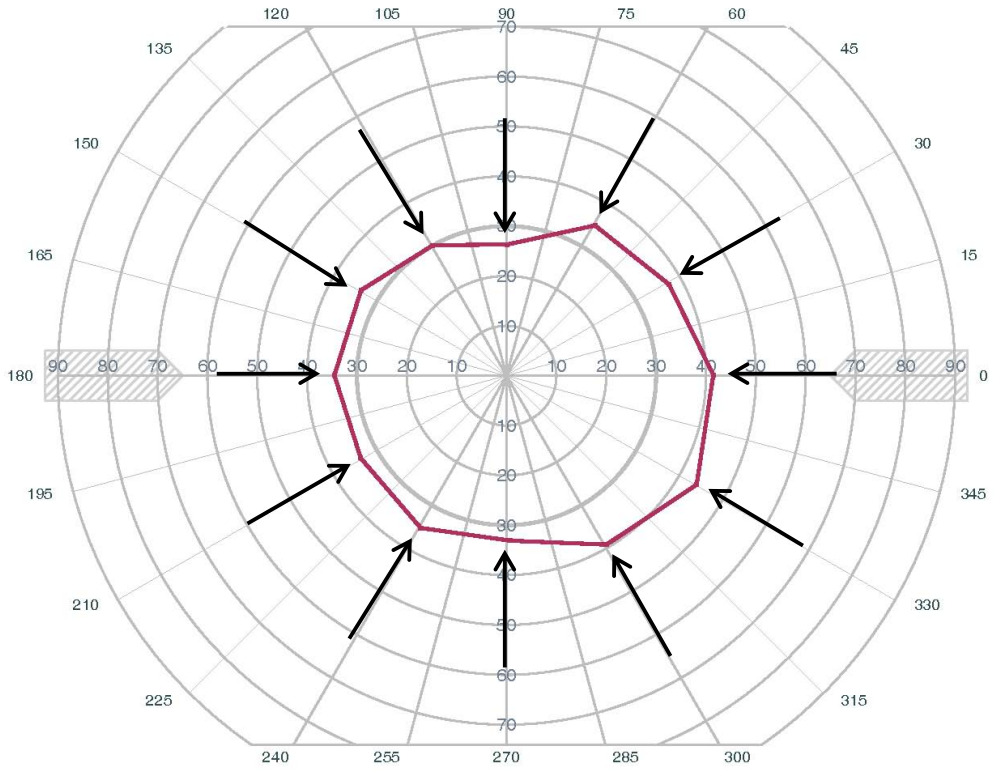

Figure 1. Presentation of stimuli every 30°

For those children who can tolerate further testing, additional points can be tested, in a non-randomised order along meridians 15° adjacent to the cardinal points starting with nasal field locations. This 'filling in' between test points allows for more accurate plotting of visual field shape, up to a maximum of 24 points per isopter.

The test procedure starts with plotting an outer isopter, followed by inner isopter and then finally the plotting of the blind spot, with the I2e stimulus (at a speed of 2°/sec).

Test points can be re-plotted if the examiner feels the initial response is unreliable i.e. the child loses fixation during the stimulus presentation, searches for stimuli, fails to respond or presses for the noise of stimulus presentation. This accommodates temporary lapses in co-operation, but repeat testing should not be undertaken in those with persistently poor co-operation.

As soon as examination of the first eye is complete, the occlusion should be removed, and the child allowed a few minutes to rest, whilst the assessment of the second eye is prepared.

Clear instructions

Instructions to patients have a significant effect on reliability and repeatability. This can be minimised by clear instructions to the patients by the perimetrist as to what is to be done and how they should respond. These should be given before each test.

"We're going to look at the [white/green] light in the middle of the bowl. For the test, you need to watch the [white/green] light all the time and try not to look anywhere else. There will be a little white light that looks like this (demonstrate stimulus), that moves in from the side, and you just need to press your buzzer as soon as you see the light."

[Confirm instructions have been understood]

"Can you test the buzzer for me now?"

[Subject presses buzzer]

Set child in the correct position, and begin familiarisation task.

"We're going to start with a quick practice, so you know what to look for."

[Inform child when test begins]

Allow the child to "sit back and relax" between isopters and demonstrate the next stimulus before re-aligning at the chinrest. Only one practice presentation is necessary for the next isopter.

The following sections highlight potential changes in test procedure for children of different ages.

Children aged 5-7 years
In this age group, you should expect to plot two isopters, with 12-15 points per isopter. Most children will struggle to plot an accurate blind spot.

Approximately 75% of children will be able to achieve a 'good quality' EBAR test rating with Goldmann perimetry. Fewer children (<50%) will be able to perform to the same standard using Octopus perimetry.

Children aged 8-11 years

In this age group, you should expect to plot two isopters, with 18-24 points per isopter. Some children may struggle to plot an accurate blind spot.

Approximately 75% of children will be able to achieve a 'good quality' EBAR test rating.

Children aged 12+ years

In this age group, you should expect to plot two or more isopters, with 18-24 points per isopter and subjects can demonstrate adult-like responses. Isopter choice should allow for maximum coverage of the visual field.

Approximately 75% of children will be able to achieve a 'good quality' EBAR test rating.

Interpretation of findings

Visual field test results should be compared to age-matched normative data provided in the OPTIC study templates (available from: http://e-lucid.com/i/video_and_images/optic_templates.html).